

Screening for and Management of Opioid Use Disorder in Older Adults in Primary Care



Rajat Duggirala, MD^a, Sunil Khushalani, MD, DFAPA^b,
Todd Palmer, MD^c, Nicole Brandt, PharmD, MBA, BCGP, BCPP^{d,e,f},
Abhilash Desai, MD^{g,h,*}

KEYWORDS

- Opioid • Older • Elderly • Addiction • Naloxone • Buprenorphine • Methadone • Naltrexone

KEY POINTS

- Prevention of Opioid use disorder (OUD) is much easier than treatment, best done by trying to avoid the use of opioids for chronic pain, and if prescribed, using the lowest possible dose for the shortest possible duration.
- Routine screening for OUD is recommended for all older adults, especially in primary care as it may result in earlier diagnosis, earlier treatment, and reduced morbidity, mortality, and healthcare costs.
- Suspect OUD in patients with characteristic symptoms and signs, especially if they have risk factors, and provide brief intervention, referral if needed, and treatment if possible.
- Evidence shows that Medications for OUD (MOUDs) are very effective in reducing opioid use and in reducing mortality even when used without psychosocial interventions and should not be withheld in patients who refuse or unable to obtain psychosocial interventions.
- Combination of psychosocial behavioral approaches that are age-sensitive along with MOUD are the treatments of choice.

^a Saint Louis University, 1438 South Grand Boulevard, St Louis, MO 63104, USA; ^b Kolmac Outpatient Recovery Centers, 3919 National Drive, Suite 300, Burtonsville, MD 20866, USA; ^c Addiction Fellowship, Family Medicine Residency of Idaho, 777 North Raymond Street, Boise, ID 83704, USA; ^d MedStar Center for Successful Aging, 220 Arch St, 12th Floor, Baltimore, MD 21201, USA; ^e University of Maryland School of Pharmacy; ^f The Peter Lamy Center on Drug Therapy and Aging; ^g Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, 413 North Allumbaugh Street, Suite#101, Boise, ID 83704, USA; ^h Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine

* Corresponding author.

E-mail address: dr.abhilashdesai@icloud.com

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INTRODUCTION

Opioid misuse (OM) describes a broad clinical syndrome of using opioids without a prescription or in doses and frequencies greater than prescribed, and for purposes other than its medical use.¹ Data collected from 2006 to 2013 found that 35% of adults older than 50 years reported OM in the past 30 days.² OM is often associated with untreated or undertreated pain in older adults and often co-occurs with misuse of other illicit drugs such as marijuana.³ OM in older adults leads to severe physical and psychiatric morbidity.⁴

Opioid use disorder (OUD) is a clinical diagnosis involving the compulsive use of opioids despite negative consequences and can be thought of as a subset of OM.¹ OUD is a chronic relapsing disease.⁵ This diagnosis is becoming more common in older adults.^{6,7} With effective treatment of OUD, a cohort of adults with early onset OUD in their twenties and thirties are now aging well into their sixties. Other older adults may also develop OUD later in life in association with prescribed opioids for their chronic pain.⁶ Older adults with OUD have higher mortality rates from an accidental overdose, suicide, and violent death compared with their peers without OUD.⁸ Additionally, they may be less likely than younger adults to perceive OUD as problematic or to access specialty treatment services.⁹

In general, meeting the unique needs of older adults with OUD will need efforts at all levels of care in health-care systems and range from prevention to intervention and treatment. Reimbursement systems must support a spectrum of approaches that include safe and appropriate opioid prescribing practices, screening for and early detection of OUD, diagnosis, treatment, and ongoing management of patients with OUD.¹ Primary care providers (PCPs) are on the front lines of these efforts illustrated through four patient cases. This clinical review describes the screening, for as well as the management of OM in general, and OUD specifically as applied to primary care.

SCREENING, BRIEF INTERVENTION, AND REFERRAL FOR TREATMENT

Screening, brief intervention and referral for treatment is an approach and a framework designed to systematize and standardize the practice of screening for and addressing substance misuse.⁵ While research has primarily identified its effectiveness in hazardous levels of alcohol use, it has applications in identifying OUD and the risk of OUD. Suspect OUD in older adults with characteristic symptoms and or signs, especially if they have risk factors. Please refer to [Table 1](#) and [Box 1](#).^{1,5,6}

Screening

The Federal Substance Abuse and Mental Health Administration (SAMHSA) recommends at least annual screening for substance misuse, including prescription medications such as opioids.⁶ Screening should also occur when major life changes occur for older adults or when family members raise concerns about an older adult's medication or other substance use. [Table 2](#) lists screening tools that may be used in primary care.^{10–15} None of the screening tools listed are as yet validated in older adults. PCPs should communicate the results of a positive screen in a respectful and culturally sensitive manner, emphasizing that an OUD is not a negative judgment but a clinical diagnosis. For patients with a past history of OUD who screen negative, praising them for maintaining abstinence is also important. In high-risk patients (eg, past history of heroin addiction and current mental health challenges), a drug screen (eg, random urine drug screen) is recommended as an additional tool for clinical data.⁶ PCPs need to address stigma of addiction at the time of screening. Stigma of

	OUD	Opioid intoxication	Opioid withdrawal
Signs	<ul style="list-style-type: none"> • Recurrent visits to emergency department for opioid related adverse effects, especially respiratory and or central nervous system depression • Family members noticing frequent drowsiness and or slurred speech in patients on opioids • Use of opioid medications at great frequency or amount than prescribed • Any and all use of illicit opioids • Use of prescription opioids for reasons other than pain management (eg, for its euphoric effects, to “manage” stress, anxiety, depression or dysphoria) 	<ul style="list-style-type: none"> • Bradycardia • Head nodding • Hypokinesia • Hypotension • Hypothermia • Miosis^a • Respiratory depression • Sedation • Slurred speech • Hypoactive delirium 	<ul style="list-style-type: none"> • Diaphoresis • Hyperreflexia • Hypertension (mild) • Hyperthermia • Tachycardia (mild) • Increased respiratory rate • Lacrimation • Muscle spasms • Mydriasis • Piloerection • Rhinorrhea • Yawning • Agitation • Restlessness • Shivering • Sneezing • Tremor
Symptoms	<ul style="list-style-type: none"> • Difficulty remembering and thinking • Difficulty staying awake in the daytime • Fatigue • Tiredness 	<ul style="list-style-type: none"> • Analgesia • Calmness • Euphoria 	<ul style="list-style-type: none"> • Abdominal pain and cramps • Leg cramps • Anxiety • Bone and muscle pain • Diarrhea • Anorexia • Nausea/vomiting • Dizziness • Restless leg syndrome

^a Normal pupillary size does not rule out opioid toxicity.

Data from Olsen Y, Sharfstein JM. The opioid epidemic: what everyone needs to know: Oxford University Press, 2019; and Adults SAO. Treatment Improvement Protocol (TIP) Series, No. 26. Center for Substance Abuse Treatment. Rockville (MD): Substance Abuse and Mental Health Services Administration (US) 1998.

addiction may make it less likely that older adults will spontaneously share their problems with opioids and accept referrals for treatment.

Brief Intervention and Referral

Education is a key component of brief intervention. Please refer to [Table 3](#).^{1,5,6} Partnering with family and concerned significant others using a culturally competent approach and assessing beliefs, attitudes, and expectations about OUD treatment is key to successful outcomes in older adults. PCPs should explain to patients and their families that OUD is a medical condition (brain disorder) and not a moral defect. PCPs should explain the serious risks associated with opioid use ([Table 4](#)), especially risk of overdose death.^{1,5,6,16–18} Person-first language should be used, and diligent effort is needed to not use stigmatizing and traumatizing language ([Table 5](#)).^{1,6}

Box 1**Key risk factors for opioid misuse and opioid use disorder in older adults**

- Long-term opioid therapy for chronic noncancer pain
- Past history of opioid misuse or opioid use disorder
- Current or past history of other substance misuse and or substance use disorder (eg, benzodiazepines, hypnotics, marijuana)
- Family history of substance use disorders and or psychiatric disorders
- History of psychiatric disorders
- History of adverse childhood experiences or history of severe trauma

Data from Olsen Y, Sharfstein JM. The opioid epidemic: what everyone needs to know: Oxford University Press, 20196; and Joshi P, Shah NK, Kirane HD. Medication-assisted treatment for opioid use disorder in older adults: an emerging role for the geriatric psychiatrist. *The American Journal of Geriatric Psychiatry* 2019;27(4):455-57.

PCPs should provide education about recognizing opioid overdose and responding to overdose (including effective use of naloxone) to patients, their family, housemates, and friends. PCPs need to help the patient see that accepting treatment is a sign of strength rather than vulnerability.

PCPs should also tackle the ageism (stigma of aging) from the start. It is a myth that older adults do not benefit from OUD treatment. Not only do older adults benefit from medications for opioid use disorder (MOUDs), age-sensitive psychosocial behavioral interventions and family support but they achieve better treatment outcomes than their younger counterparts.^{6,19}

PCPs should educate patients and their families that although addiction counseling and mutual-aid support groups are core components of OUD treatment, they are generally not effective by themselves and that OUD treatment should include MOUD.⁶ For most patients who screen positive for OUD, PCPs should make a referral

Table 2**Screening tools for opioid use disorder in primary care**

Situation	Screening tools	Clinical pearls
Routine screening	NIDA quick screen (National Institute for Drug Abuse)	Excellent screening tool for nonopioid drug misuse and use disorder also
Before initiating LTOT ^a	SISAP questionnaire (Screening instrument for Substance Abuse Potential) Opioid risk tool (ORT) DIRE score (Diagnosis, Intractability, Risk and Efficacy)	SISAP and ORT are very brief and easy to use DIRE score is more comprehensive and recommended over SISAP and ORT
In patients on LTOT	SOAPP-R (Screener and Opioid Assessment for Patients with Pain – Revised) COMM (Current Opioid Misuse Measure)	Both, SOAPP-R and COMM are equally good

^a LTOT: Long-term Opioid Therapy for management of chronic pain.

Data from Refs. ^{10–15}

Education of patient and family/ support persons	Clinical aspects	Team member
OM and OUD are serious chronic brain disorders	Address stigma and shame	Nurse Social worker PCP Psychiatrist ^a
Adverse effects of opioids	Discuss impact of opioids on current meds and medical – psychiatric comorbidity	PCP Pharmacist ^a
Need for routine periodic screening, what screening involves and Importance of honest answers during screening	Involvement of family/support persons is key to accurate early diagnosis	Nurse Social worker PCP
Importance of naloxone in preventing overdose death, and how and when to use it	Explain signs and symptoms of overdose (eg, impaired arousal, respiratory depression [especially respiratory rate <12/ min], miosis, cyanosis, hypothermia, seizures, aspiration pneumonia)	Nurse Social worker PCP Pharmacist
Education about local, national and internet-based resources	Mutual aid support groups are a key example	Nurse Social worker Peer support specialist

^a Psychiatrist and pharmacist may be available virtually as part of collaborative care.

Data from Olsen Y, Sharfstein JM. The opioid epidemic: what everyone needs to know: Oxford University Press, 20196; and Joshi P, Shah NK, Kirane HD. Medication-assisted treatment for opioid use disorder in older adults: an emerging role for the geriatric psychiatrist. The American Journal of Geriatric Psychiatry 2019;27(4):455-57.

to local opioid treatment centers for accurate diagnoses (not just of OUD but also co-occurring substance use disorders [especially alcohol, Benzodiazepines, and marijuana in older adults] and mental health conditions) and comprehensive holistic treatment. SAMHSA-certified programs can exist in intensive outpatient, residential, and hospital settings. Services include treatment of medical opioid withdrawal management, initiation of MOUDs in combination with a variety of psychiatric, behavioral, social, and medical interventions. Older adults do best if opioid treatment centers provide age-appropriate care by providers who are knowledgeable about issues related to aging (6). Motivational interviewing techniques can help PCPs address the patients' ambivalence or reluctance to accept the problem and treatment referral. Providing a wide range of resources (eg, contact information of local addiction treatment centers, local mutual-support group networks, geriatric care managers, reputable online resources, SAMHSA National Helpline [800-622-HELP]) for the patient, as well as for the caregivers (eg, Nar-Anon) is a key component of education and brief intervention. PCPs should also provide emotional support to family and suggest self-care techniques to mitigate burnout. In addition, geriatric psychiatrists can play a key role in prevention and treatment of OUD in older adults by working closely and collaboratively with PCPs as illustrated in care of Ms. T.²⁰

Table 4		
System-based adverse effects of opioids		
System	Adverse effects	Clinical pearls
General	Fatigue Opioid Induced hyperalgesia (OIH) Tolerance Diversion	OIH requires lowering of opioids (increasing opioids worsen pain) Tolerance to analgesic effects may require increase in opioids which in turn may cause more adverse effects
Psychiatric	Addiction (opioid misuse [OM], opioid use disorder [OUD]) Physiologic Dependence Psychological Dependence Withdrawal syndrome Euphoria (immediate effect) Depression (long-term effect) Hallucinations	Individuals with other substance misuse and substance use disorders (current or past) have increased risk of developing OM and OUD Individuals with pre-existing depression and or psychotic disorders are at increased risk of these adverse effects Methadone withdrawal psychosis has been described
Respiratory	Respiratory depression Hypoxia Sleep disordered breathing	Opioids may exacerbate COPD, sleep apnea syndromes, asthma and other pulmonary conditions In palliative and end-of-life settings, opioids may be needed to treat dyspnea
Neurocognitive	Inattention Memory impairment Mental cloudiness Impaired abstract thinking Disorientation Delirium	Individuals with pre-existing mild cognitive impairment or dementia are at higher risk of these adverse effects Individuals on anti-cholinergic medications are at higher risk of these adverse effects Frail older adults are at increased risk of fatigue, falls and injury.
Sleep wake cycle	Daytime sleepiness Nightmares	Individuals with pre-existing OSA and other sleep disorders are at higher risk of these adverse effects
Endocrine	Sexual dysfunction Decreased testosterone levels Amenorrhea Reduced bone mineral density Increased prolactin levels	Individuals with pre-existing osteopenia and osteoporosis may have worsening of their condition with correspondent increased risk of fractures
Urinary	Urinary retention (UR) Urinary incontinence (UI)	Individuals with pre-existing UR and UI are at increased risk of these adverse effects
Neurologic	Incoordination Slurred speech Impaired vision Dizziness Loss of fine motor skills Falls and injury (eg, TBI, fractures)	Individuals with pre-existing neurologic conditions (eg, stroke, TBI, Parkinson's disease) are at increased risk of these adverse effects Opioids can impair driving abilities and this adverse effect needs to be inquired and monitored

(continued on next page)

System	Adverse effects	Clinical pearls
Gastrointestinal	Constipation Intestinal obstruction Anorexia Nausea Vomiting Dry mouth	Individuals with pre-existing gastrointestinal problems (eg, previous abdominal surgeries) are at higher risk of these adverse effects
Dermatologic/Skin changes	Pruritis Rash Diaphoresis	Older adults are often given anticholinergic medications to treat pruritis (eg, hydroxyzine, diphenhydramine) putting them at further risk of cognitive impairment and delirium
Cardiovascular	Hypotension Arrhythmias	Methadone prolongs QTc interval more so than other opioids and so should be avoided in older adults with pre-existing cardiac conduction problems. Involvement of a pharmacist is recommended to identify any and all medications that also prolong QTc interval

Data from Refs. ^{1,6,16–18}

CASE 1: MS. T

Ms. T is a 77-year-old retired nurse currently residing in a nursing home receiving long-term opioid therapy (LTOT) for severe chronic pain from multiple conditions, including shoulder osteoarthritis following prior cervical spondylosis and diabetic neuropathy. She also has multiple sclerosis that has started to involve her diaphragm and lung volumes. She is prescribed long-acting morphine 30 mg three times a day, tramadol

Person-first language	Stigmatizing and traumatizing language
Person with substance use disorder	Addict, Drug abuser, Junkie, Drug seeker, Pill seeker
Person in recovery	Former addict
Drug misuse; Harmful use	Drug abuse
Substance use disorder	Drug habit
Being abstinent, being sober, not using, testing positive for substance use or consistent with abstinence	Being “clean” or “dirty” or “negative for substance use”
Heavy substance use over short time	Drug binge
Medications for Opioid Use Disorder	Opioid replacement therapy

Data from Olsen Y, Sharfstein JM. The opioid epidemic: what everyone needs to know: Oxford University Press, 20196; and Adults SAAO. Treatment Improvement Protocol (TIP) Series, No. 26. Center for Substance Abuse Treatment. Rockville (MD): Substance Abuse and Mental Health Services Administration (US) 1998.

100 mg every 6 hours as needed for pain, and lorazepam 0.5 mg daily as needed for anxiety. She has been asking for more pain medication as her pain is “not at all” controlled. Through virtual collaborative psychiatric care with a geriatric psychiatrist, Ms. T is diagnosed with mild OUD. Ms. T is educated about OUD and safely transitioned from morphine to buprenorphine 2 mg (along with naloxone) three times a day. Her tramadol and lorazepam are tapered off and duloxetine (for management of chronic pain) and cognitive behavior therapy for pain is initiated.

ROLE OF NALOXONE

PCPs should routinely prescribe naloxone to older adults with OUD to reduce the risk of opioid overdose death.¹ In addition, patients and/or caregivers may be able to obtain naloxone as permitted by the individual state through prescriptions, directly from a pharmacist, or as part of a community-based program. Naloxone is a strong affinity, full, competitive mu-opioid receptor antagonist and thus displaces opioid agonists, thereby reversing their effects.²¹ Naloxone administration intranasally or parenterally (intramuscular, intravenous, subcutaneous) is the standard of care to reverse respiratory and central nervous system (CNS) depression that is known or suspected to be caused by an opioid overdose and thus prevent fatal overdose. Naloxone is life-saving in these situations, and information has been issued by the Food and Drug Administration (FDA) to increase its use. It has a short half-life (2 hours) and thus, its effect although rapid and complete, is short-lasting (30–90 minutes).²¹ Multiple doses of naloxone may be needed particularly when the overdose is caused by high potency opioids, like fentanyl.²¹ A naloxone drip may be required to maintain safe respiration, especially if long-acting opioids (eg, methadone) have been used. Naloxone precipitates opioid withdrawal so that the person on waking up generally begins to experience distressing withdrawal symptoms.²¹ PCPs should prescribe naloxone to patients with OUD and give prescriptions to their family, friends, and housemates after educating them about when and how to use it.¹ It is recommended that patients and people in close contact with them carry naloxone on their person for quick access if needed. After every situation that required naloxone administration in the community, emergency medical services should be activated to include emergency department care.⁵

OPIOID WITHDRAWAL MANAGEMENT

Opioid withdrawal produces extreme discomfort and hence medically managed opioid withdrawal is recommended.⁷ This is generally done in an in-patient or residential setting but can also be safely done in an outpatient setting via telehealth. Symptoms include sweating, shaking, chills, body aches, yawning, large pupils, headache, craving, nausea, vomiting, abdominal cramping, diarrhea, insomnia, agitation, depression, anxiety, and other behavioral changes that can last for days to weeks¹ (see [Table 1](#)). Clinical opiate withdrawal scale may be used to monitor withdrawal symptoms.²² Fear of withdrawal is a significant deterrent to stopping opioid use. Opioid withdrawal does not lead to delirium, so the presence of delirium suggests withdrawal of another substance (eg, benzodiazepines, alcohol).⁶ In older adults, other causes of delirium (eg, infection) should also be looked for. The goal of withdrawal management in the context of OUD is to have a short period of withdrawal allowing for titration of buprenorphine or methadone that the patient can be stabilized and maintained on for relapse prevention.⁶ If the patient chooses not to be on maintenance buprenorphine or methadone, then the goal of withdrawal management is to achieve a complete sustained withdrawal before adding naltrexone for relapse prevention.

Symptoms typically begin within 8 hours, peak at 48 to 72 hours, and resolve within 7 days.²³ Long-acting opioids (eg, methadone, fentanyl) may have delayed onset, delayed peak, and longer duration of withdrawal symptoms. A substantial proportion of individuals may have protracted withdrawal symptoms for additional 6 months.²⁰ Symptoms of menopause (eg, night sweats, achy joints) may be confused with that of opioid withdrawal.²⁴

Nonopioid medications for symptomatic treatment include clonidine for treatment of sympathetic overactivity (eg, tachycardia, elevated blood pressure), loperamide for diarrhea, dicyclomine for abdominal cramps, nonsteroidal anti-inflammatory drugs (NSAIDs) for joint and muscle pain, and trazodone for insomnia. Muscle relaxants, antiemetics, and anxiolytics may also be used.⁶ Lofexidine is approved by the FDA for the treatment of OUD and its mechanism of action is similar to clonidine. High cost of lofexidine is a barrier to its routine use. Successful opioid withdrawal by itself is not sufficient treatment and may paradoxically increase the risk of overdose, as well as a quick relapse if it is not followed by a comprehensive treatment of OUD that includes MOUD.¹

Use of medications used to manage withdrawal carries an increased risk in older adults due to the prevalence of multiple serious multiple medical comorbidities.⁷ PCPs can play a key role in collaboratively working with addiction treatment providers to ensure safe withdrawal management and minimize the risks of medications routinely used for the treatment of opioid withdrawal. For example, NSAIDs can also cause gastrointestinal bleeding, heart failure, and renal impairment in the elderly, and this needs to be carefully considered with their use.

MEDICATIONS FOR OPIOID USE DISORDER

Evidence shows that MOUDs (buprenorphine and methadone) are very effective in reducing opioid use and in reducing mortality even when used without psychosocial interventions and should not be withheld in patients who refuse or unable to obtain psychosocial interventions.^{6,25} For some patients, medical management may suffice.²⁵ The FDA has approved three medications for the treatment of OUD: buprenorphine, methadone, and naltrexone.²⁶ These three medications together constitute MOUDs. Previously, the terms used were Medications for Addiction Treatment or Medication Assisted Therapy. Buprenorphine and methadone together constitute Opioid Agonist Therapy for OUD.

PCPs need to educate patients and family that methadone and buprenorphine do not produce a euphoric high in individuals with OUD due to the high tolerance to opioids that these individuals have developed and due to the unique pharmacodynamic and pharmacokinetic properties of these two opioids.¹ They instead minimize withdrawal symptoms and cravings, thereby promoting the normal functioning of the individual with OUD in relationships and activities of daily living. These medications are best seen as harm-reduction strategies. Most patients with OUD need MOUD for several years and some (eg, severe heroin addiction) for decades. The ultimate goal may be to wean the patient off these maintenance medications, but this decision needs to be made in collaboration with the patient, family, and team members.⁷ Tapering of these medications needs to be done very slowly, over months or even years in some cases, only when there has been functional recovery, and when there are no ongoing significant psychosocial stressors or unstable comorbid conditions. Otherwise, the risk of relapse is considerable.¹

In opioid-naïve patients, overdose-related deaths can occur with buprenorphine and methadone but is quite uncommon with buprenorphine use.⁶ It mainly can happen

with concurrent use of CNS depressants, primarily benzodiazepines. Overdose death with methadone is more of a concern which is greatly heightened by concurrent use of benzodiazepines and/or alcohol. Like other opioid medications, buprenorphine and methadone are sometimes diverted and misused.¹ Use of higher doses increases the risk of diversion.⁵ Some diversion also occurs as patients try to manage withdrawal symptoms on their own. Diversion of methadone is more common with methadone prescribed for the treatment of pain than for the treatment of OUD. Buprenorphine and methadone control cravings better than naltrexone and hence are associated with better outcomes than naltrexone treatment, especially related to mortality reduction.^{1,5} Patient's preference regarding the choice of MOUD needs to be considered.

BUPRENORPHINE

Buprenorphine is a high-affinity, partial mu-opioid agonist with slow dissociation, resulting in a lower risk of creating euphoria and lower risk of overdose death compared to full agonists.¹ It is approved by the FDA for the treatment of OUD. It is also used for opioid withdrawal management and pain management.²⁷ For OUD treatment and withdrawal management, it can be given once a day. For pain management, it may need to be given in three to four divided doses a day as its analgesic effect may wear off in 6 to 8 hours.¹

Buprenorphine may be preferred over methadone and naltrexone for OUD treatment in older adults except in patients with injectable heroin-related OUD.¹ Buprenorphine has less risks than full opioid agonists (eg, oxycodone, morphine, fentanyl), but it is still a potent opioid with all the risks associated with opioid use listed in [Table 1](#), and thus considered a high-risk medication in older adults.⁷

Unlike methadone, buprenorphine can be prescribed by PCPs in primary care and other office-based settings in the treatment of OUD, whereas methadone can only be used to treat OUD in federally qualified opioid treatment centers. Buprenorphine (being a partial agonist) can precipitate opioid withdrawal if receptors are bound by full agonists (heroin, prescription opioids) at the time of administration (Refer to case 2).¹ It should be started once opioid withdrawal symptoms develop in patients with OUD. Buprenorphine has a ceiling effect, and this can be a barrier to the treatment of individuals with higher opioid tolerance. In these individuals, initial transition to methadone and then to buprenorphine may be considered. It has higher affinity for mu-opioid receptors than other opioids and so impedes further opioid binding.⁵ So, if a patient takes heroin or prescription opioids while on buprenorphine, they are unlikely to experience any euphoric effects. Buprenorphine does not require adjustment in individuals with renal failure. Compared with methadone, less is known about buprenorphine safety in older adults.¹ It is preferable to methadone because it is less likely to cause withdrawal symptoms, erectile dysfunction, constipation, and respiratory depression.^{1,6}

For OUD treatment, the combination of buprenorphine and naloxone is preferred to buprenorphine alone to minimize the risk of diversion and intravenous self-administration and subsequent respiratory and CNS depression.¹ Older adults who have a significant decline in physical health or get transitioned to long-term care setting may be appropriate for taper and discontinuation of buprenorphine with continued close monitoring for relapse (eg, cravings are returning).⁷

Formulations and Dosing

Buprenorphine is available as buccal film, sublingual tablets, transdermal, long-acting injectable (weekly and monthly formulation) and 6-month buprenorphine subdermal

implant.⁶ Buprenorphine in combination with naloxone is available as buccal film (under the tongue or inside the cheek) and sublingual tablets. Naloxone has minimal bioavailability when taken buccally or sublingually, and hence it does not block the effect of buprenorphine unless taken parenterally.⁵ Initial dosing begins with 2 mg in older adults (in combination with naloxone 0.5 mg) and, if well tolerated, the dose may be increased if withdrawal symptoms and/or cravings are not controlled. The final dose is generally lower in older adults than that needed for younger individuals. In younger individuals, the average dose range needed is around 16 to 24 mg once daily.

CASE 2: MS. S

Ms. S is a 61-year-old grandmother who relapsed on heroin after 5 years of recovery. Ms. S wants to babysit her granddaughter. Ms. S's daughter-in-law would not allow her to babysit until Ms. S was "clean." A friend of Ms. S offered her a buprenorphine film to help her get off heroin. Ms. S did not know much about buprenorphine and took it. After the first dose, she experienced severe heroin withdrawal symptoms. She called her PCP who informed her that buprenorphine could precipitate withdrawal and needed to be taken once withdrawal symptoms developed. PCP treated Ms. S's withdrawal symptoms and referred her to an outpatient opioid addiction treatment program in the community for comprehensive treatment along with MOUDs.

METHADONE

Methadone is a full mu agonist (1). It is approved by the FDA for treatment of OUD. It is also used to manage opioid withdrawal and for chronic, severe treatment refractory to pain.²⁷ For OUD treatment and withdrawal management, it can be given once a day. For pain management, it may need to be given in three to four divided doses a day (despite its long half-life) as its analgesic effect may wear off in 6 to 8 hours.¹ Patients receiving methadone for OUD cannot rely on once-a-day dosing for pain relief.

Methadone is a long-acting opioid. A dose on average lasts 24 to 36 hours (even longer in older adults).¹ Owing to its long half-life and its extremely variable and idiosyncratic dose response, it carries a higher risk of opioid overdose and overdose death compared with other opioids.²³ Owing to its NMDA receptor antagonistic activity, it may be used for opioid-induced hyperalgesia (OIH), as dysfunction in NMDA receptor activity has been implicated in the development of OIH.⁶ Other opioids do not have NMDA antagonist property.²⁷ Methadone is relatively safe in individuals with renal failure compared with morphine for chronic severe treatment-refractory pain management. Methadone may be preferred over buprenorphine and naltrexone for older adults with severe OUD due to injectable opioid use¹ (Refer to Case 3).

The number of older adults in methadone treatment for OUD is growing.²⁰ Many older adults may be on methadone treatment for decades. Hence, although PCPs may not be prescribing methadone for OUD, they will need to learn the unique risks and benefits of methadone use in older adults.⁷ Its use is associated with a significant reduction in opioid or illicit opioid cravings and does not cause euphoria in individuals with heroin addiction because it outcompetes heroin for opioid receptor binding.¹ This property also helps reduce heroin overdose and heroin overdose deaths because much of the effects of heroin are blocked by methadone.

Owing to the risk of drug–drug interactions, long half-life (and thus accumulation) and prolongation of QTc (and thus risk of arrhythmias), the use of methadone in older adults carries more risks than in younger adults and more risks compared with buprenorphine.^{7,18} Pretreatment EKG and repeat EKG after 1 month of treatment with methadone are recommended. Owing to its long half-life, its idiosyncratic,

variable, and unpredictable dose-response, and relatively shorter time taken to cause respiratory depression compared with pain relief, dangerous respiratory depression can occur if the dose is prematurely increased instead of waiting for 5 to 7 days or longer to reach a steady state. Because of the higher risk of sedation compared with buprenorphine, it should be avoided in older adults with severe respiratory or cardiac disease.^{1,17}

Formulation and Dosing

Methadone is available as tablets and liquid. For OUD, it is given in the liquid form.⁶ For pain, it is generally given in the tablet form, and the prescription should state that methadone is for pain.¹ For OUD, initial dosing in older adults should begin with 10 mg. The dose is slowly increased, and the final dose is generally lower than that needed for younger individuals. In younger individuals, doses of 100 mg of methadone or higher is not unusual.

CASE 3: MR. L

Mr. L is a 68-year-old nursing home resident, a retired veteran with chronic severe noncancer pain (due to multiple back surgeries, sciatica, arthritis). He also has a past history of heroin addiction, opioid overdose, and prescription misuse. Mr. L is on oxycodone 20 mg three times daily plus oxycodone 10 mg with acetaminophen 325 mg combination pill as needed every 6 hours for breakthrough pain. He has a long history of demanding more and more opioids for pain control. After his best friend recently passed away, he has been asking for all the as-needed medications almost every day. Through virtual collaborative psychiatric care with a geriatric psychiatrist, Mr. L is safely transitioned from oxycodone (both scheduled and as needed) to methadone 20 mg three times daily. Venlafaxine (for management of chronic pain) and grief counseling are initiated. The social worker helps Mr. L get connected to a local mutual aid support group and a peer support specialist.

NALTREXONE

Naltrexone is approved by the FDA for treatment of OUD, as well as alcohol use disorder (AUD).⁶ For older adults with both OUD and AUD, naltrexone may be preferred over buprenorphine and methadone. Naltrexone is a full opioid antagonist. It is long acting and may be given every 2 to 3 days, especially in older adults although it is recommended as once-daily administration.²³ It should not be used in older adults requiring prescription opioids for pain relief. Naltrexone may precipitate significant opioid withdrawal symptoms in those taking opioids. To treat OUD, it is generally given at least 7 to 10 days after a medically supervised opioid withdrawal, and 10 to 14 days if withdrawing from buprenorphine or methadone.¹ This period is a high-risk period for relapse and thus, robust social support and use of psychological interventions are recommended to prevent relapse during this period.

Although high-quality studies of its use for OUD in older adults are lacking, naltrexone was found to be safe and effective for the treatment of AUD in older adults.²⁸ Nonadherence is more common with oral naltrexone than with buprenorphine or methadone and hence injectable once a month formulation is preferred. (Refer to Case 4).⁵ Before giving long-acting injectable naltrexone, a trial of oral naltrexone should be considered to ensure that there is little risk for withdrawal symptoms or an allergic reaction. Naltrexone may cause liver dysfunction and hence PCPs should avoid naltrexone prescription in older adults with acute hepatitis or liver failure.²⁶

Formulation and Dosing

Naltrexone is available as once-daily pill, as well as once a month injection (380 mg once a month), although the pill form is generally not recommended for the treatment of OUD mainly because of adherence issues compared with the injectable form. Typically, 25 mg naltrexone should be taken on day one and if it is tolerated well, from day two onwards 50 mg daily is recommended.

CASE 4: MR. A

Mr. A is a 66-year-old retired construction worker who has prescription OUD. His son wants him to get help but also tells him that he should not get on Suboxone (buprenorphine-naloxone combination pill) because that would be replacing one addictive drug with another addictive drug. Mr. A does not want methadone because he has seen a friend of his taking it and his friend has been partly nonadherent and in addition, at times his friend appears intoxicated. The PCP discusses the option of naltrexone and Mr. A agrees to a monthly injection of long-acting naltrexone.

BOLSTERING SOCIAL SUPPORT

Social support is critical to achieving and maintaining long-term recovery from OUD in older adults.¹ PCPs should diligently work to strengthen existing social networks and creating new networks. The latter includes recovery-oriented social networks (eg, mutual-aid support groups, peer recovery support specialists).⁷ PCP should clarify the level of involvement of family and other support systems the patient would like to involve them throughout the treatment journey.

Mutual-aid support groups (eg, Narcotics Anonymous, Self-Management and Recovery Training, Celebrate Recovery) consist entirely of people who volunteer their time and typically have no official connection to addiction treatment centers.⁵ Such groups support abstinence and foster new social connections, a sense of belonging, and healthy lifestyles. Mutual-aid support groups may be critical to recovery for patients who cannot access treatment due to a lack of adequate health insurance coverage for addiction treatment.²⁵

Older adults who take methadone may experience even more social isolation than older adults with other types of SUDs.²⁴ Older adults who have used opioids for many years may have severed ties with family and friends and lost friends who overdosed. People who take methadone may perceive significant stigma about their history of opioid use and their treatment from friends, family, and society.¹ Key reasons older adults with OUD may self-isolate are past experiences of being taken advantage of, fear of future loss, wish to avoid grief over the loss of family/friends, and past experiences of domestic violence.⁷ It is recommended that PCPs have social workers in their practice who can address these concerns preemptively so that PCPs can then collaboratively work with their patients to build a nonopioid-using social network that supports MOUD as a pathway to recovery. Social workers can also help connect patients to peer-support specialists who can share their own experiences with addiction and recovery and also connect them to other resources; all of which have significant value.

ADDRESSING CO-OCCURRING DISORDERS

Identifying and treating all co-occurring disorders (not just optimal pain control) is essential if older adults with OUD are to achieve overall wellness.⁷ PCPs can play a key role in optimally addressing co-occurring disorders. Older adults with OUD have a higher prevalence of depression, delirium, and dementia compared with older adults

without OUD.²⁹ Older adults on methadone for OUD have higher rates of arthritis, hypertension, human immunodeficiency virus (HIV), and hepatitis C (HCV) compared to younger peers.^{30,31} Opioids and naltrexone are metabolized by the liver and hence, their use in older adults with liver disease should be done with extreme caution and very low doses may need to be used. Caution is also needed in use of opioids in older adults with respiratory disorders (eg, chronic obstructive pulmonary disorder [COPD], obstructive sleep apnea [OSA], obesity hypoventilation syndrome, asthma).^{7,17} Injection opioid use (eg, heroin) is the primary driver of the HIV and Hepatitis C epidemic. MOUDs can reduce HIV and HCV prevalence by reducing risk behaviors in people who inject heroin and other opioids. MOUDs also improve outcomes of HIV and HCV infection by promoting adherence to HIV and HCV treatment.¹

LTOT is defined as the use of opioids on most days for more than 3 months.³² There is no study that supports the use of LTOT for chronic noncancer pain.^{27,32} There is one study that found LTOT for chronic moderate to severe hip, knee or back pain to be no better than nonopioid therapy and carried more risks than nonopioid therapy.³³ Hence, LTOT should be prescribed only in rare situations where the pain is severe, chronic, and treatment-refractory, and only if the benefits outweigh risks¹ based on the patient's medical and psychiatric comorbidity. Use of patient agreement forms are recommended before initiating LTOT.

Concurrent use of opioids and benzodiazepines and opioids and gabapentinoids (gabapentin, pregabalin) amongst 65 years and older is prevalent, generally prescribed by the same PCP, and poses a higher risk of overdose death, especially opioids and benzodiazepines.^{1,27,34} Deprescribing of CNS depressants used concomitantly with opioids (eg, benzodiazepines, gabapentin, pregabalin, muscle relaxants, sedating antipsychotics [eg, quetiapine, olanzapine]) should be considered routinely.

Accidental overdose has been described in individuals taking both opioids and benzodiazepines, and this risk is even higher in individuals with certain medical comorbidities (eg, COPD, OSA).⁷ Older adults also tend to misuse multiple medications (eg, opioids, benzodiazepines, hypnotics, muscle relaxants).^{27,35} This in turn increases the risks of serious health consequences including death. PCPs should be diligent in avoiding the co-prescription of opioids and benzodiazepines and minimizing co-prescription of opioids and gabapentinoids.

SUMMARY

Managing OUDs in older adults takes a team due to multiple co-morbidities, polypharmacy, as well as limited supports. PCPs need to be vigilant in recognizing signs and symptoms, as well as taking preventative efforts. Ongoing advocacy is needed to support the reimbursement not only of medications but of supportive services. Expanded telehealth services need to be maintained in order to support older adults especially in medically underserved communities.

CLINICS CARE POINTS

- Primary care providers (PCPs) need to develop competency and confidence in prescribing as well as monitoring the use of buprenorphine and other treatment approaches for older adults with Opioid Use Disorder (OUD).
- Initiation of buprenorphine generally requires an interval of time without other opioids and development of some degree of opioid withdrawal symptoms, whereas initiation of naltrexone requires a much longer interval and opioids to be fully out of the system to avoid precipitated withdrawal.

- Concurrent use of opioids and benzodiazepines should be avoided because of the greatly increased risk of overdose and death, and prescribing opioids with any other medications or substances with central nervous system depressant properties (e.g., gabapentinoids, muscle relaxants, hypnotics, alcohol) also carries increased risk of overdose and death, and thus should be done with great caution or avoided.
- PCPs should educate patients and their family/friends/housemates regarding the use of naloxone and prescribe naloxone routinely for all patients who are prescribed opioids and for those who have OUD.

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