Primary care management of adults with opioid use disorder

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INTRODUCTION

In the United States, opioid use disorder (OUD) has fueled a national crisis of overdose deaths and other opioid-related harms. OUD affects people who use prescription opioids, as well as those who use heroin or other illicit opioids, especially illicitly manufactured fentanyl. Clinicians encounter people with OUD throughout the health care system, and each point of care can represent an important opportunity to make an OUD diagnosis, offer evidence-based treatment, and connect an individual with ongoing care. Caring for people with OUD is an essential part of primary care, where, as with other chronic health conditions, it can be managed with a long-term treatment plan. This chapter reviews key issues in providing primary care to people with OUD, including the management of common comorbid conditions.

Issues related to opioid misuse and OUD in adults are reviewed in detail in other topics:

- (See "Opioid use disorder: Epidemiology, clinical features, health consequences, screening, and assessment".)
- (See "Opioid use disorder: Treatment overview".)
- (See "Opioid use disorder: Pharmacologic management".)
- (See "Opioid use disorder: Psychosocial management".)

- (See "Management of acute pain in adults with opioid use disorder".)
- (See "Opioid use disorder: Overview of treatment during pregnancy".)
- (See "Prescription drug misuse: Epidemiology, prevention, identification, and management".)
- (See "Opioid withdrawal: Medically supervised withdrawal during treatment for opioid use disorder".)
- (See "Prevention of lethal opioid overdose in the community".)

DEFINITIONS

Person-centered terminology should be used when caring for people with opioid use disorder (OUD). Stigmatizing language (eg, "substance abuser," "addict") perpetuates negative perceptions and attitudes among clinicians and is a commonly cited barrier as to why people with OUD are not engaged in treatment [1,2]. We advise that clinicians use the following terms when evaluating and counseling patients and their supports regarding OUD.

- **Addiction** – The American Society of Addiction Medicine defines addiction as a treatable, chronic medical illness involving complex interactions among neural circuits, genetics, the environment, and an individual's life experiences [3]. People with addiction suffer from a problematic pattern of substance use and compulsive behaviors that often continue despite harmful physical and/or psychosocial consequences.
- **Substance use disorder (SUD)** – In the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), "substance use disorder" (SUD) is a single diagnostic category that replaced two separate diagnoses of substance abuse and dependence [4]. The diagnosis of SUD can be specific to a substance, including opioids, stimulants (eg, cocaine), sedative-hypnotic-anxiolytics (eg, benzodiazepines), and alcohol.
- **Opioid use disorder (OUD)** – According to the DSM-5, a diagnosis of OUD is ascertained when at least 2 of 11 clinical criteria are met within a 12-month period (table 1). Tolerance and withdrawal are part of the diagnostic criteria for OUD in general, but not applicable to prescribed opioid use that is supervised under a clinician. OUD severity can range from mild to severe, which can help guide treatment planning.
- **People with opioid use disorder** – The term "people with opioid use disorder" models the person-first language that is standard when referring to people living with chronic medical

conditions.

- **Medications for opioid use disorder (MOUD)** – The term "medications for opioid use disorder" (MOUD) refers to the three opioid agonist or antagonist medications that are approved by the US Food and Drug Administration to treat OUD: buprenorphine, methadone, or naltrexone.

  Although the term "medication-assisted treatment" is commonly used to describe SUD treatment programs that offer medications, the authors advise using the term "MOUD" because medications reflect evidence-based treatments, not just as adjunctive to behavioral therapies. MOUD are integral to the long-term treatment for persons with OUD, rather than being an ancillary or short-term treatment.

EPIDEMIOLOGY

- **Prevalence** – In the 2019 National Survey on Drug Use and Health (NSDUH), the prevalence of any substance use disorder (SUD) among the United States population age 12 and older is approximately 7.7 percent, or 19.3 million people [5]. The prevalence of opioid use disorder (OUD) is relatively low in the context of all SUD; in 2019, an estimated 1.6 million people in the United States had OUD. Among people with OUD, approximately 0.5 million have heroin-related OUD, while 1.4 million have opioid analgesic-related OUD. However, the NSDUH is a household survey that may miss people who are incarcerated, not housed, or living in other unstable arrangements. Therefore, some estimates of heroin use are more than five times greater than those reported in the NSDUH [6]. (See "Opioid use disorder: Epidemiology, clinical features, health consequences, screening, and assessment", section on 'Epidemiology'.)

- **Mortality** – From 1999 to 2018, the age-adjusted rate of opioid-involved overdose deaths nearly quadrupled in the United States [7]. The biggest driver of overdose deaths has been synthetic opioids (other than methadone), in particular illicitly manufactured fentanyl, where the number of attributable overdose deaths swelled from 0.3 to 9.9 per 100,000 standard population from 1999 to 2018. The rate of heroin-related overdose deaths also rose sharply from 1999 to 2017, from 0.7 to 4.9 per 100,000. During this time, overdose deaths involving natural and semi-synthetic opioid analgesics, such as oxycodone and hydrocodone, increased from 1.0 to 4.4 per 100,000. Altogether, opioids accounted for 71 percent of the 70,630 drug overdose deaths in the United States in 2019 [8]. (See "Prevention of lethal opioid overdose in the community", section on 'Prevalence'.)

- **Health care utilization** – Opioid-related emergency department visits, hospital admissions, and related health care costs increased rapidly over the last two decades. In the United States, opioid-related emergency department visits rose by almost 100 percent between 2005 and 2014 [9]. Between 2001 and 2012, heroin overdose-related and prescription opioid-related admissions increased by 1.9- and 2.5-fold respectively; these overdoses accounted for $5.5 billion USD in cumulative hospitalization costs.

  In addition, skin and soft tissue infections related to intravenous and/or subcutaneous/intramuscular opioid use was associated with a doubling of hospital admissions from four to nine per 100,000 between 1993 and 2010 [10]. Estimated annual hospital admissions for intravenous drug use-associated infective endocarditis increased from 2900 cases in 2013 to more than 20,000 cases in 2017 [11].

- **Medications for opioid use disorder (MOUD)** – Mortality among people with OUD is markedly reduced by treatment with MOUD [12], including methadone, naltrexone, and buprenorphine. Initiation of methadone or buprenorphine as MOUD after non-fatal opioid overdose is associated with a 38 to 59 percent reduction in opioid-related mortality [13]. In addition, continuing methadone or buprenorphine treatment is associated with a reduction in all-cause mortality compared with discontinuing treatment (25 and 4 fewer deaths per 1000 person-years for methadone and buprenorphine treatment respectively) [14]. (See "Opioid use disorder: Pharmacologic management".)

  Evidence-based treatment with MOUD remains underutilized. In 2019, of the 1.6 million people with estimated past-year OUD, only 18 percent reported any receipt of MOUD within the last 12 months [5]. Only 36 percent of specialty substance use treatment facilities in the United States provided any MOUD as of 2016; of these, only 29 percent offered methadone despite its proven efficacy [15]. Conversely, buprenorphine treatment expanded substantially in the primary care setting, with the rate of buprenorphine prescribing increasing from 1.3 to 2.7 people per 100,000 population from 2010 to 2018 [16].

PRIMARY CARE MANAGEMENT

Approach to the patient — Patients with opioid use disorder (OUD) are a heterogeneous group of people with a wide range of health problems and other care needs. Some patients may be able to maintain stable employment and relationships, while others may have impaired psychosocial functioning with difficulties addressing their chronic health and social issues.

Thus, "meeting the patient where they are" is essential to creating an effective provider-patient relationship. Clinicians, as well as office staff, must take a nonjudgmental approach in all interactions with patients who use drugs, and avoidance of stigmatizing language and assumptions about substance use will encourage honest and open communication. Patients may be seeking care for an acute illness or management of chronic medical conditions, but they may not wish to discuss or address their substance use with care providers. Understanding the patients' reasons for accessing care is an essential first step in establishing goals of care.

Clinicians should be aware of, assess, and consider certain psychosocial issues that are more commonly seen in patients with OUD, including:

- Stigma, which may affect self-disclosure of substance use and motivation for medications for opioid use disorder (MOUD)
- Competing priorities that may interfere with engagement in care for chronic health conditions
- Trauma, including physical and psychological trauma
- Violence, including being a victim of or witness to sexual, interpersonal, family, and community violence
- Housing instability or homelessness
- Exchange of sex for money or drugs
- Current or prior legal issues, including incarceration
- Inadequate psychosocial supports

Routine and preventive care — Regardless of a patient's substance use, participation in OUD treatment, or openness to engaging in treatment, all patients should receive appropriate management of acute and chronic medical conditions as well as general preventive care, including:

- Follow-up of all chronic health problems.
- Guideline-based preventive health screening and administration of recommended vaccinations. (See "Overview of preventive care in adults" and "Standard immunizations for nonpregnant adults" and "Immunizations during pregnancy".)
- Evaluation and provision of contraceptive and reproductive care, if applicable. (See "Contraception: Counseling and selection".)
- Medication reconciliation to identify potential drug-drug interactions that can occur with MOUD, particularly methadone (eg, antiretrovirals, anticonvulsants) (table 2) [17]. Methadone can alter electrical conduction within cardiac tissue leading to QT prolongation

and torsades de pointes. The evaluation of patients taking methadone is reviewed in detail elsewhere. (See "Opioid use disorder: Pharmacologic management", section on 'Methadone: Opioid agonist'.)

- Evaluation of and counseling on medication adherence.
- Referral and assistance with social needs such as food insecurity and housing instability.

Specific care concerns for patients with opioid use disorder

Assessment of opioid use — Clinicians should inquire about and document substance use and treatment history, as well as potential issues related to treatment (form 1). These include (see "Opioid use disorder: Epidemiology, clinical features, health consequences, screening, and assessment" and "Substance use disorders: Clinical assessment"):

- Types, amount, frequency, and duration of opioid and other substance use; differentiate between opioids obtained from prescriptions versus other nonmedical sources.
- What was the longest period of abstinence? What contributed to the most recent period of abstinence or use?
- When was the last use, and are there any withdrawal symptoms?
- Route of use; if injecting, what equipment is the individual using? Are sterile syringes being used, and how are they being obtained?
- Overdose history; has the individual experienced slowed breathing or loss of consciousness with substance use? Have they administered or been administered naloxone?
- Current and prior treatment history; what MOUD, if any, have been tried previously (methadone, buprenorphine, or naltrexone)? What treatment settings have been tried (eg, residential treatment, intensive outpatient counseling, opioid treatment programs)? Attendance in mutual-help groups (eg, 12-step programs)?

Risk-factor directed care — In addition to all routine age-based preventive care recommendations, clinicians should assess the other health care needs of people with OUD based upon possible comorbidities and risk factors, such as co-occurring substance use disorders (SUD), mental health conditions, injection drug use (IDU), sex work, homelessness, and incarceration. Specific health care issues include:

Infectious disease complications

- Screening for, offering pre- or postexposure prophylaxis for, and treating human immunodeficiency virus (HIV) infection.

  - Screening – Guidelines from the Centers for Disease Control and Prevention recommend at least annual HIV screening for people who inject drugs and for other people with OUD and elevated HIV risk [18]. (See "Screening and diagnostic testing for HIV infection", section on 'Whom to test'.)

    Although the incidence of HIV infection among people who inject drugs has dropped from its peak in the 1980s, increasing IDU during the past decade has put many United States counties at high risk for HIV outbreaks [19]. In 2018, IDU accounted for 1 in 15 new HIV infections, with almost 50 percent occurring in individuals ages 13 to 34 years [20].

  - Prophylaxis – Pre- and postexposure HIV prophylaxis for people who inject drugs is discussed in detail elsewhere. (See "Management of nonoccupational exposures to HIV and hepatitis B and C in adults" and "HIV pre-exposure prophylaxis", section on 'Persons who inject drugs'.)

  - Treatment – Ongoing substance use is not a contraindication to antiretroviral therapy [21]. Despite advances in antiretroviral medications, marginalized groups, including people who inject drugs, have experienced smaller reductions in HIV-related mortality than others [22]. Assuring access to antiretroviral therapy is critical for people with OUD.

    In addition to other factors that contribute to antiretroviral therapy choice, simplicity of treatment (eg, single pill regimens), hepatotoxicity, and drug-drug interactions are important considerations for people with OUD. Some first- and second-line regimens contain medications that interact with methadone and potentially buprenorphine through induction of cytochrome P450 (CYP3A4). In particular, some non-nucleoside reverse transcriptase inhibitors (eg, efavirenz) can increase methadone metabolism and may require increases in methadone dose to avoid opioid withdrawal symptoms (table 3). (See "Overview of antiretroviral agents used to treat HIV" and "Selecting antiretroviral regimens for treatment-naïve persons with HIV-1: General approach".)

- Screening and vaccination for hepatitis A and B, and screening for hepatitis C. (See "Hepatitis B virus: Screening and diagnosis in adults" and "Hepatitis B virus immunization in adults" and "Screening and diagnosis of chronic hepatitis C virus infection" and "Hepatitis A virus infection: Treatment and prevention".)

- Screening – Guidelines from the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America recommend that all people who inject drugs be offered annual hepatitis C virus (HCV) testing with HCV antibody (or HCV viral load if the patient has a history of prior infection) (algorithm 1) [23].

  Transmission of HCV primarily occurs parenterally, which makes IDU a common risk factor for HCV infection. The incidence of acute HCV infection increased between 2004 and 2017 in the United States due to an increase in IDU [24,25], with IDU accounting for at least 60 percent of acute HCV infections [23]. In one study including three cohorts of people who inject drugs in four United States cities, more than one-third became infected with HCV within five years of IDU initiation [26].

  The equipment used for intranasal insufflation ("snorting") of opioids can also carry and transmit HCV; therefore, people using opioids intranasally should also be offered periodic HCV testing [25].

- Treatment – HCV treatment can be offered concomitantly with MOUD. In a clinical trial of 301 people with HCV who were receiving MOUD, 12 weeks of elbasvir-grazoprevir resulted in cure (sustained virologic response at 12 weeks) in 92 percent of those treated immediately and 90 percent of those receiving delayed treatment [27]. In this clinical trial and another including patients receiving MOUD, substance use during HCV treatment was not associated with worse treatment outcomes [27,28]. Integrating HCV treatment into MOUD treatment programs is feasible and effective [29,30]. Instruments are available to assess psychosocial factors that may affect adherence to HCV medications [31], but HCV treatment should not be withheld based upon substance use alone. (See "Patient evaluation and selection for antiviral therapy for chronic hepatitis C virus infection", section on 'Active drug use'.)

- Other medical problems related to IDU, such as bacterial infections (endocarditis, osteomyelitis, abscess) and pulmonary complications:

  - Skin and soft tissue infections, infectious endocarditis, and other systemic infections are common among people who inject drugs [11,32,33]. Abscesses and cellulitis can often be treated in the primary care setting, while more serious infections, such as bacterial endocarditis, osteomyelitis, or necrotizing fasciitis, usually require hospitalization. Pulmonary infections, including pneumonia, may also be associated with illicit or prescribed opioid use [34]. (See "Pathogenesis of osteomyelitis" and "Vertebral osteomyelitis and discitis in adults" and "Acute cellulitis and erysipelas in adults: Treatment" and "Overview of pulmonary disease in people who inject drugs".)

- Screening for and treatment of latent tuberculosis (see "Tuberculosis infection (latent tuberculosis) in adults: Approach to diagnosis (screening)" and "Treatment of tuberculosis infection (latent tuberculosis) in nonpregnant adults without HIV infection"):

  - Some individuals with OUD are at increased risk of latent tuberculosis, particularly those who are experiencing homelessness or are residents or staff of homeless shelters, residents or staff of correctional facilities, or health care workers (table 4). If a decision to treat is made, clinicians should be aware that methadone can interact with the rifamycins (eg, rifampin) (see "Rifamycins (rifampin, rifabutin, rifapentine)", section on 'Drug interactions') and recommend an alternative tuberculosis treatment regimen, adjustment in methadone dose, or change from methadone to buprenorphine. (See "Treatment of tuberculosis infection (latent tuberculosis) in nonpregnant adults without HIV infection", section on 'Selecting a regimen'.)

- Screening for and prevention of sexually transmitted infection, including syphilis, gonorrhea, and chlamydia. (See "Screening for sexually transmitted infections", section on 'Risk groups' and "Prevention of sexually transmitted infections".)

Coexisting substance use disorders

- Screening for alcohol and other substance use, and offering treatment for coexisting SUDs (see "Screening for unhealthy use of alcohol and other drugs in primary care"):

  - OUD frequently co-occurs with other SUDs, including alcohol use disorder. Identifying and treating other SUDs are essential components of OUD care; validated instruments such as the Alcohol Use Disorders Identification Test (AUDIT-C) and the Substance Use Brief Screen (SUBS) can be used in the primary care setting as screening tools (table 5 and table 6) [35]. Decisions to initiate treatment for comorbid SUDs should be patient-centered, and there is little evidence to support delaying treatment of other SUDs to focus on OUD treatment. Addressing co-occurring SUDs concomitantly may improve treatment outcomes for both conditions [36-38].

    Naltrexone is approved by the US Food and Drug Administration for treatment of both alcohol use disorders and OUD and can be used to treat both conditions concomitantly [39]. Because naltrexone is an opioid antagonist, it is contraindicated for patients receiving methadone or buprenorphine treatment. Administering naltrexone to patients taking any opioid agonist medications would lead to opioid withdrawal; initiation of naltrexone for OUD therefore requires an adequate period of abstinence from opioids, which may be challenging for patients. While few studies have directly compared methadone, buprenorphine, and naltrexone for OUD treatment, the

strength of evidence supporting methadone and buprenorphine is greater than that supporting naltrexone [13,40-42]. Thus, we consider methadone and buprenorphine as first-line treatment options for patients with OUD, even for those with comorbid alcohol use disorder. However, the long-acting injectable formulation of naltrexone can be a convenient option for some patients with both OUD and alcohol use disorder. (See "Alcohol use disorder: Treatment overview" and "Opioid use disorder: Pharmacologic management", section on 'Approach to treatment'.)

Additionally, benzodiazepine use disorder is common among people with OUD and is strongly associated with opioid overdose mortality due to the potential of prolonged and severe respiratory depression that can occur with coadministration of both agents [43]. Although concurrent benzodiazepine and opioid use increases overdose risk [44], buprenorphine and methadone can be safely administered to patients who take benzodiazepines with careful monitoring [45]. The risks of patient harm from withholding MOUD are greater than the risks of coadministering these medications with benzodiazepines. However, we refer patients with benzodiazepine use disorder to opioid treatment programs that can provide additional monitoring during MOUD. (See "Benzodiazepine use disorder", section on 'Opioid use disorder'.)

- Screening and treatment for tobacco use disorder (see "Overview of smoking cessation management in adults" and "Pharmacotherapy for smoking cessation in adults"):

  - Chronic medical conditions stemming from tobacco use, such as cardiovascular disease, stroke, and cancer, are the leading causes of death among people with OUD [46]. People with OUD infrequently receive evidence-based treatment for tobacco use disorder despite their high burden of tobacco-related illness. Though quit rates are lower among people receiving MOUD than the general population of people who smoke [47], pharmacotherapy, such as nicotine replacement therapy (NRT) and varenicline have evidence of efficacy when administered with methadone treatment:

    - In a meta-analysis including nine trials and over 1300 participants, the use of NRT during methadone treatment improved the odds of successful smoking cessation compared with placebo (odds ratio 6.32, 95% CI 1.18-33.75) [48].

    - Trials comparing the use of varenicline in patients on MOUD have shown inconsistent results. In one trial, varenicline demonstrated greater efficacy than placebo in short-term smoking cessation [49]. Another showed no significant reduction in quit rates with varenicline [46].

Further, there is no evidence that smoking cessation negatively impacts SUD treatment outcomes [37,38].

Chronic pain

- Comorbid chronic pain (see "Prevention and management of side effects in patients receiving opioids for chronic pain" and "Management of acute pain in adults with opioid use disorder", section on 'Patients receiving pharmacotherapy for opioid use disorder'):

  - There is a bidirectional relationship between opioid use and chronic pain. Chronic pain conditions are common among people with OUD, and opioid use may intensify or exacerbate chronic pain. In one study, 37 percent of patients in methadone treatment programs had chronic pain [22]. Patients who initiate prescription opioid analgesics for chronic pain are at risk for developing OUD (see "Prescription drug misuse: Epidemiology, prevention, identification, and management", section on 'Use disorder'). Further, the pharmacologic effects of opioids can contribute to chronic pain through opioid-induced hyperalgesia, in which pain sensitization is enhanced despite opioid therapy [50]. (See "Prevention and management of side effects in patients receiving opioids for chronic pain", section on 'Opioid-induced hyperalgesia'.)

    Chronic pain treatment for people with OUD should employ comprehensive multimodal approaches, including OUD treatment, nonopioid analgesics, nonpharmacologic treatments such as physical therapy, and other psychosocial treatments directed at pain and comorbid mental health conditions [51]. Patients with OUD and chronic pain are best managed through a multidisciplinary team, and primary care clinicians can coordinate a multidisciplinary approach by referring such patients, particularly those with other psychiatric comorbidities, for management with pain, addiction, and mental health specialists [52]. If a comprehensive multimodal program is unavailable, the inclusion of mental health and pain management specialists in developing a treatment plan may be beneficial.

Coexisting mental health conditions

- Co-occurring mental health conditions (see "Substance use disorders: Clinical assessment", section on 'Mental health' and "Co-occurring schizophrenia and substance use disorder: Epidemiology, pathogenesis, clinical manifestations, course, assessment and diagnosis" and "Opioid use disorder: Psychosocial management"):

  - All people with OUD should receive screening for co-occurring mental health conditions prior to initiating MOUD or during routine primary care.

OUD is associated with major depressive disorder, anxiety disorders, posttraumatic stress disorder, attention deficit hyperactivity disorder, and personality disorders [53-56]. Data are less consistent regarding the prevalence of bipolar disorder and schizophrenia among people with OUD. In studies that assessed mental health conditions in people seeking methadone treatment and those with prescription OUD, nearly one-half met criteria for at least one co-occurring mental health condition [39,53].

Making a psychiatric diagnosis in people with SUDs requires careful attention to the time course of symptoms and their relation to substance use. Chronic mental health conditions may precede or be caused or exacerbated by substance use. For example, opioids may cause mood symptoms and prolonged exposure can develop into major depressive disorder [57]. Additionally, other substance use, such as cannabis, has been associated with the development of psychosis [58]. There are also likely shared genetic or environmental vulnerabilities that put people at risk for both OUD and chronic mental health conditions [59]. Identifying symptoms that are related to substance use is critical because these symptoms may improve or resolve with the cessation or reduction of substance use.

The mainstay of treatment for co-occurring psychiatric disorders is integrated care with a single clinician or team of clinicians with expertise in both mental health and SUD treatment. The clinician or team should establish a unified patient-centered treatment plan that addresses both mental health and substance use. MOUD remains first-line treatment for patients with OUD and a co-occurring psychiatric diagnosis. Although some evidence supports psychosocial interventions such as group counseling, contingency management, and residential dual diagnosis treatment [60], there is a paucity of high-quality randomized controlled trials to support specific psychosocial interventions for people with severe mental illness and substance misuse [61].

Most medications used to treat psychiatric conditions can be used safely in patients on MOUD, although prescribers should be aware of the potential for additive sedation and QT prolongation, particularly for patients on methadone. (See "Opioid use disorder: Pharmacologic management", section on 'Adverse effects'.)

Harm reduction interventions — Harm reduction refers to interventions aimed at reducing the negative effects related to substance use or other potentially harmful health behaviors [62]. Harm reduction does not condone or condemn substance use; a clinician who practices harm reduction discusses the harms of substance use with the patient and identifies strategies to reduce associated harms. Examples of common harm reduction interventions include

designated driver campaigns to reduce morbidity associated with driving while intoxicated and condom use to prevent sexually transmitted infections or pregnancy.

We offer harm reduction interventions to all patients with OUD, regardless of their engagement with OUD treatment. For OUD, harm reduction interventions include prescribing of naloxone to prevent opioid overdose and referral to syringe service programs to reduce infections associated with unsafe injection. Harm reduction interventions can reduce the morbidity and mortality associated with OUD [63-70] and, in addition, may serve to build provider-patient rapport. Patients with OUD should be encouraged to continue their efforts to limit harmful substance use.

The following harm reduction approaches can be employed in the care of patients with OUD:

- **Overdose prevention and naloxone** – We suggest that clinicians provide overdose prevention education and co-prescribe naloxone for any patient with OUD, including current and prior history of OUD. In most states in the United States, naloxone can be dispensed at a pharmacy to any individual through a non-patient-specific standing order [71]. Clinicians can also refer patients to local harm reduction service organizations that provide naloxone kits and training. A resource to identify local organizations can be found at National Harm Reduction Coalition. (See "Prevention of lethal opioid overdose in the community".)

  Overdose prevention education points include:

  - Avoid using opioids alone, particularly intravenous opioids (eg, use with a companion, and take turns)
  - Do not mix sedating substances (eg, benzodiazepines, alcohol) with opioids
  - Go slow (eg, "taste", or sample, a small amount of each new batch of opioids prior to using a larger amount)
  - Be aware that tolerance may be reduced if not using as much recently as in the past (eg, if just released from the hospital, "detox" facility, or jail) [72]
  - Educate close companions regarding the location and use of naloxone in case of overdose

The efficacy of overdose prevention including community-based naloxone and other opioid antagonists is reviewed elsewhere. (See "Prevention of lethal opioid overdose in the community", section on 'Efficacy'.)

- **Safer injection** – We suggest that clinicians provide education to patients with OUD on safer injection practices, including advice to rotate injection sites, clean the skin prior to injecting, and not to reuse syringes and needles, and referral to a syringe service program. Safer injection practices may reduce the morbidity and mortality associated with IDU and are not associated with increased drug use [73-75]. As examples:

  - In a meta-analysis including six observational studies, use of a syringe service program was associated with a decreased risk of acquiring HIV infection (risk ratio [RR] 0.42, 95% CI 0.22-0.81) [76].

  - In a 2017 systematic review including five observational studies from North America and Europe, although the availability of syringe service programs was not associated with a reduction in HCV acquisition, in certain European regions, the presence of high-coverage syringe service programs was associated with a 76 percent reduction in HCV (RR 0.24, 95% CI 0.09-0.62) [66].

  - In a retrospective study evaluating the prevalence of maternal HCV seropositivity in an Ohio county, introduction of a local syringe service program was associated with a reduction in the rate of increase in maternal HCV infections. From 2006 to 2011, the rate increased 137 percent; after the introduction of the syringe program in 2011, the rate of maternal HCV only increased 12 percent in the county over the next four years. Contiguous counties also experienced similar improvements in maternal HCV rates, while regional, noncontiguous counties continued to have elevated rates of infection [68].

  - In a randomized controlled trial including 600 people who inject drugs, use of a syringe service program was not associated with increased drug use compared with those receiving usual care [75].

  In some jurisdictions, clinicians may be able to prescribe sterile syringes, needles, and sharps containers to people who inject drugs [77]. However, in most US states, sterile syringes and injection equipment are considered illegal drug paraphernalia, even when prescribed by clinicians or accessed from pharmacies. As such, authorized syringe service programs play an important role in many communities. Syringe service programs provide sterile needles, syringes, injection supplies, and often other health-promoting services (eg, HIV testing) to registered participants. Clinicians can refer to organizations such as National Harm Reduction Coalition or their local health departments for more information about syringe services programs in their area.

Overdose prevention centers, also known as supervised injection sites, are sanctioned facilities that allow people to consume preobtained drugs under the supervision of trained staff. They are intended to reduce harms associated with drug consumption, and they have been associated with positive outcomes in countries around the world [78]. The first sanctioned overdose prevention center in the United States opened in New York City in 2021 [79].

MANAGING MEDICATIONS FOR OPIOID USE DISORDER IN PRIMARY CARE

Care for people with opioid use disorder (OUD) can be optimized by integrating medications for opioid use disorder (MOUD) into the primary care setting.

For many people with OUD, this is preferred, likely because of familiarity, accessibility, and lower stigma associated with integrated primary care addiction treatment [80]. Receipt of MOUD in primary care is associated with high patient satisfaction [81], particularly in the context of strong patient-provider relationships and a supportive patient-centered care environment. Referral to specialty substance use treatment programs, however, may be appropriate for people with more intensive mental health or psychosocial needs, as additional supports and services may be available through these programs (see "Substance use disorders: Determining appropriate level of care for treatment"). However, for some individuals, referral to an outside program may be unsuccessful due to lack of access or challenges with patient engagement, and as a result leave some without OUD treatment.

Primary care clinicians should inquire if patients are receiving MOUD outside of the primary care setting. In addition, clinicians should review state prescription drug monitoring programs (PDMPs) for buprenorphine prescriptions as well as other opioids and non-opioid controlled substances dispensed through community pharmacies. Of note, methadone and buprenorphine dispensed through opioid treatment programs are not routinely listed on PDMPs; federal amendments permitting PDMP reporting by opioid treatment programs were enacted in 2020, although reporting of these medications is not mandatory.

For patients receiving MOUD from another provider, collaboration between providers is ideal. Clinicians may need to review records of prior substance use treatment to help inform current treatment planning. Clinicians should be aware that federal law (42-CFR-Part 2) protects the confidentiality of substance use treatment records at specialty treatment programs, and written consent from a patient must be obtained to access, review, and discuss details specific to substance use treatment outside of primary care settings.

Initiating MOUD — When offering to initiate MOUD, the primary care clinician may best frame concerns about the individual's substance use in terms of specific health risks. Many people who use drugs are ambivalent about their use. Even if treatment is initially declined, the clinician should continue to highlight the availability of MOUD at future appointments because the patient may accept treatment at some point. (See "Substance use disorders: Motivational interviewing".)

Primary care clinicians should consult and be familiar with national guidelines and implementation guides for the delivery of MOUD in office-based settings, including primary care. Examples include:

- Integrating Buprenorphine Treatment for Opioid Use Disorder in Primary Care
- Provider Clinical Support System: Clinical Tools
- Boston Medical Center Office Based Addiction Treatment Training and Technical Assistance
- The American Society of Addiction Medicine National Practice Guideline For the Treatment of Opioid Use Disorder
- SAMHSA Medications for Opioid Use Disorder
- SAMHSA Buprenorphine Quick Start Guide

Buprenorphine and naltrexone are the primary MOUD modalities that can be prescribed in the primary care setting since methadone treatment for OUD must be delivered through federally regulated opioid treatment programs. Patients with OUD who need more intensive services than can be provided through primary care settings can be referred to a local opioid treatment program or other specialty substance use treatment programs. In the United States, opioid treatment programs are the only settings through which patients with OUD can access methadone treatment; they also provide individual and/or group counseling. Common reasons why patients may benefit from referral outside of primary care include preference for or prior success with methadone treatment; unstable, co-occurring severe mental illness; or severe alcohol or benzodiazepines use disorder that can benefit from closer monitoring and intensive services. (See "Substance use disorders: Determining appropriate level of care for treatment" and "Opioid use disorder: Treatment overview".)

Telemedicine visits can also be employed to deliver care for people with MOUD, although this has generally been limited to rural health settings where travel distances between the patient and provider may be prohibitive [82]. Federal regulations limiting telemedicine for

buprenorphine treatment initiation were waived under the declaration of public health emergency for coronavirus disease 2019 (COVID-19). Subsequently, the use of telemedicine for MOUD delivery was expanded into nonrural health settings [83,84], although outcomes have not been rigorously evaluated [85,86].

Maintaining MOUD — For patients receiving MOUD, primary care clinicians should acknowledge OUD as a chronic medical condition at all visits. As with any chronic medical problem, the clinician should inquire about recent control or problems with opioid use, including cravings and relapse. Additionally, the clinician should ask about any changes in MOUD therapy and side effects; the buprenorphine dose can be titrated according to the patient's symptoms (see "Opioid use disorder: Pharmacologic management", section on 'Buprenorphine: Opioid agonist'). Patients who are undergoing buprenorphine titration or are experiencing side effects should have close follow-up (eg, within two to four weeks). Otherwise, for patients doing well on a stable dose, without significant cravings or relapse, the clinician may space out follow-up visits and provide interim refills.

- **Toxicology testing** – When treating OUD, toxicology tests (saliva or urine) may provide important clinical information to complement patients' self-report and provider assessment. Clinical guidelines recommend the use of toxicology tests in addiction treatment; however, evidence that support the use of toxicology testing in improving patient outcomes is limited [87]. Clinicians should be thoughtful in the use of these tests to maintain a patient-centered rather than a punitive treatment approach. Many providers have limited knowledge on the interpretation of toxicology results [88], and the use of toxicology may introduce disparities in care, as racial biases are evident in the ordering of these tests [89]. When considering toxicology tests, clinicians should:

  - Understand the test characteristics, costs, and indications for toxicology tests. As examples, synthetic opioids require tests that are specific to the opioid (eg, methadone, buprenorphine, oxycodone, and fentanyl are not detected with screening tests for "opiates" but require specific screening and/or confirmatory tests for each of them) (table 7). Guidance on toxicology interpretation is available and should be part of the clinical toolkit for OUD treatment in primary care [90-93]. (See "Testing for drugs of abuse (DOAs)".)

  - Set clear expectations with patients about how toxicology tests fit in as a component of their treatment plan. Having transparent discussions about how to navigate unexpected (ie, positive) toxicology results is essential as a part of ongoing treatment. Continued use of illicit opioids may occur even after initiating MOUD. While some patients may benefit from referral to a more intensive treatment setting, maintenance

of MOUD should not be solely dependent on negative toxicology testing. (See "Opioid use disorder: Treatment overview".)

- **Concerns over medication diversion** – Clinicians may have concerns over medication diversion, which is selling or sharing prescribed medication with someone other than the individual for whom it was intended. Buprenorphine diversion does occur; however, diversion of buprenorphine occurs at similar rates as other commonly prescribed medications. In the general population, commonly diverted medications include allergy medications, antibiotics, and opioid analgesics [94]. Relative to the diversion of full opioid agonists, however, diversion of buprenorphine, a partial agonist, is less common [95,96]. More importantly, buprenorphine diversion may occur because of the lack of access to buprenorphine treatment. For example, many individuals with OUD who are not enrolled in a formal treatment program have difficulty affording or locating available providers [97-99]; they report taking diverted buprenorphine to manage opioid withdrawal or in other ways consistent with therapeutic use [100].

  While there are no evidence-based ways to prevent diversion, primary care clinicians can implement the following practical strategies to mitigate diversion:

  - Treatment agreements that explicitly discuss expectations of buprenorphine treatment, as well as consequences for diversion activity
  - Close follow-up for patients who are new or unstable in treatment (ie, short duration between scheduled visits)
  - Limit the amount of medication per prescription for patients who are new or unstable in treatment
  - Offer long-acting formulations such as injectable buprenorphine
  - Have transparent discussions with patients that prioritize harm reduction as well as medication refills and safe storage

Managing medication side effects — Constipation is a common side effect of opioid agonist medications and may affect quality of life. In clinical practice, most constipation from methadone or buprenorphine treatment can be managed with fiber supplementation or prokinetic or osmotic laxatives (eg, bisacodyl, senna, or polyethylene glycol); peripherally acting mu-opioid receptor antagonists are usually not necessary [101]. (See "Management of chronic constipation in adults".)

Optimizing psychosocial support for MOUD — The delivery of MOUD can be enhanced through engagement of a multidisciplinary team that includes prescribing clinicians and clinical coordinators; these coordinators are key to supporting patients and can facilitate medical and

behavioral health needs. Additional team members may include nurses, pharmacists, or social workers who are integrated in the primary care setting.

Participation in counseling and other psychosocial treatment modalities should also be explored with the patient. Clinical trials that established buprenorphine efficacy delivered in the primary care setting have used a standardized but focused approach to psychosocial counseling [102,103]. A typical approach will include 15 minutes of counseling delivered by a primary care clinician or a care coordinator addressing current substance use, OUD symptoms, and relapse prevention [104]. In randomized controlled trials, more intensive psychosocial counseling has not been shown to improve buprenorphine treatment outcomes in comparison with medication management alone [105-107]. However, many people initiating buprenorphine treatment request and may benefit from additional psychosocial counseling [108]. In combination with MOUD, participation in psychosocial treatment can be important for people with co-occurring mental health conditions. Further, the primary care clinician can enhance patient rapport by addressing the patient's experience with psychosocial treatment in addition to managing MOUD.

Other patients may choose participation in mutual-help groups such as 12-step programs which provide peer-based psychosocial support. As with other psychosocial treatments, asking questions about the patient's experience in the program (eg, group attendance, presence of a sponsor, commitment to a home group) will emphasize the clinician's interest in the patient's use of peer support systems. Clinicians should be aware that some mutual self-help groups may perpetuate stigmatizing attitudes toward MOUD [109], and asking patients about this can be helpful. All patients should be encouraged to continue MOUD because premature cessation of MOUD can increase overdose risk [110,111].

Psychosocial treatments for OUD are reviewed in detail elsewhere. (See "Opioid use disorder: Psychosocial management".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Opioid use disorder and withdrawal".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Prescription drug misuse (The Basics)" and "Patient education: Opioid use disorder (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **Engage patients in opioid use disorder (OUD) treatment** – OUD affects people who use prescription opioids, as well as those who use heroin or other illicit opioids, especially illicitly manufactured fentanyl. Each point of clinical care can represent an important opportunity to make an OUD diagnosis, offer evidence-based treatment, and connect an individual with ongoing care. Person-centered terminology should be used when caring for people with OUD; stigmatizing language (eg, "substance abuser," "addict") perpetuates negative perceptions and attitudes and is a commonly cited barrier to why people with OUD are not engaged in treatment. (See 'Introduction' above and 'Definitions' above.)

- **Routine health care and specific care issues for adults with opioid use disorder** – Regardless of a patient's substance use, participation in OUD treatment, or openness to engaging in treatment, all patients should receive appropriate management of acute and chronic medical conditions as well as general preventive care. Clinicians should inquire about and document substance use and treatment history, as well as potential issues related to treatment (form 1). Clinicians should also assess other health care needs based upon possible comorbidities and risk factors, such as co-occurring substance use disorders (SUD) and mental health conditions, injection drug use (IDU), sex work, homelessness, and incarceration. (See 'Routine and preventive care' above and 'Specific care concerns for patients with opioid use disorder' above.)

- **Harm reduction interventions for all patients** – We offer harm reduction interventions to all patients with OUD, regardless of their engagement with OUD treatment. We suggest overdose prevention interventions (including education and naloxone prescriptions) (**Grade 2B**), as well as safer-injection interventions (including patient education and referral to a syringe service program) (**Grade 2C**). Harm reduction interventions reduce the morbidity and mortality associated with OUD and are not associated with increased drug use. (See 'Harm reduction interventions' above.)

- **Medications for opioid use disorder (MOUD) in the primary care setting** – Care for people with OUD can be optimized by integrating MOUD into the primary care setting. Primary care clinicians should consult and be familiar with national guidelines and implementation guides for the delivery of MOUD in office-based settings. Certain patients may benefit from referral outside of primary care, such as those with a preference for or prior success with methadone treatment; and those with unstable, co-occurring severe mental illness or severe alcohol or benzodiazepines use disorder that can benefit from closer monitoring and intensive services. (See 'Managing medications for opioid use disorder in primary care' above.)

- **Optimize psychosocial support** – The delivery of MOUD can be enhanced through engagement of a multidisciplinary team that includes prescribing clinicians and clinical coordinators; these coordinators are key to supporting patients and can facilitate medical and behavioral health needs. Participation in counseling and other psychosocial treatment modalities should also be explored with the patient. (See 'Optimizing psychosocial support for MOUD' above.)

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