



Identification and Management of Opioid Use Disorder in Primary Care: an Update

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Abstract

Purpose of Review The rising prevalence of opioid use disorder (OUD) and related complications in North America coupled with limited numbers of specialists in addiction medicine has led to large gaps in treatment. Primary care providers (PCPs) are ideally suited to diagnose and care for people with OUD and are increasingly being called upon to improve access to care. This review will highlight the recent literature pertaining to the care of patients with OUD by PCPs.

Recent Findings The prevalence of patients with OUD in primary care practice is increasing, and models of office-based opioid treatment (OBOT) are evolving to meet local needs of both ambulatory practices and patients. OBOT has been shown to increase access to care and demonstrates comparable outcomes when compared to more specialty-driven care.

Summary OBOT is an effective means of increasing access to care for patients with OUD. The ideal structure of OBOT depends on local factors. Future research must explore ways to increase the identification and diagnosis of patients with OUD, improve treatment retention rates, reduce stigma, and promote interdisciplinary approaches to care.

Keywords Opioid use disorder · Primary care · Buprenorphine

Introduction

Over the past two decades, North America has seen a dramatic rise in the prevalence of opioid use disorder (OUD) and opioid-related complications, including overdose and infection. This rise is driven largely by the increase in extra-medical use of prescription opioids in both the USA and Canada, the two countries with the highest opioid consumption in the world [1–3]. Extra-medical use of opioids refers to use of opioids in a way other than how prescribed or use without a prescription [4]. The limited availability of

specialists in addiction medicine and a system that has traditionally siloed addiction treatment into specialty centers has led to large gaps in care for the rising number of patients needing treatment for OUD [5, 6]. In response to this critical problem and facilitated by several policy changes, there has been growing attention to the importance of integrating OUD treatment into primary care [7–9]. Primary care as a site for the diagnosis and management of OUD has several advantages. First, it is the point of healthcare entry for many patients. This is important as the majority of persons with substance use disorders do not recognize and seek treatment [10••]. Second, primary care providers (PCPs) provide longitudinal care, have established relationships with their patients, and are familiar with the biopsychosocial factors that influence patient care. Third, integration of OUD treatment into primary care serves to destigmatize treatment of this chronic, relapsing condition.

Notably, in the USA, the Drug Addiction Treatment Act (DATA) of 2000 allowed PCPs to become waived to prescribe buprenorphine, a partial opioid receptor agonist, for the treatment of OUD. An amendment in 2006 and 2016 then increased the number of patients that could be treated by a PCP from 30 to 100 to 275 patients, respectively. The

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Comprehensive Addiction Recovery Act (CARA), also passed in 2016, extended the process to nurse practitioners and physician assistants [11]. Such policy changes have great potential to enhance patient access to OUD treatment in primary care settings.

In this review article, we will discuss the epidemiology of OUD in primary care, tools to screen for and identify patients with OUD, strategies for primary care-based management of OUD and associated outcomes, management of common chronic infectious comorbidities, harm reduction strategies available to PCPs, and directions for future research. We searched the literature for the past 3 years for articles relevant to the primary care treatment of patients with OUD. In areas in which the literature was scarcer, we extended the search up to 5 years.

OUD in Primary Care: General Considerations

Epidemiology

It is estimated that 1.9 million Americans have OUD related to prescription opioids, and an additional 589 thousand have OUD related to heroin (SAMHSA 2018). However, there is scarce data on the prevalence of patients with OUD already engaged in primary care, and the studies are limited by observational, self-report data. A recent multi-site study of 2000 primary care patients found that 36% may have a substance use disorder, with nearly 5% having OUD [12]. Another study of nearly 1.4 million primary care patients in six large healthcare systems found that the 13,942 (1.0%) had OUD, and among those, only 21% had received treatment with buprenorphine [13•].

OUD is likely higher among certain patient populations, such as those who use tobacco and those with other substance use disorders [14, 15]. Additionally, patients prescribed opioids for chronic pain are at risk for extra-medical opioid use and OUD. Longer duration and higher doses of prescribed opioids have been shown to be risk factors for extra-medical prescription opioid use [16, 17]. New onset extra-medical prescription opioid use has, in turn, been identified as a strong and independent risk factor for heroin initiation [18]. Patients with underlying depression and anxiety, two conditions commonly diagnosed and managed in the primary care setting, may be particularly susceptible to the development of extra-medical opioid use and OUD after the initiation of opioids for chronic pain [19, 20]. Patients with comorbid depression and pain are more likely to transition to long-term opioid therapy and to receive higher doses than those patients without depression [20].

From 2006 to 2014, there was a significant rise in primary care visits addressing OUD and since 2009 PCPs have consistently surpassed psychiatrists in terms of number of office-based visits for buprenorphine [11]. The availability of

buprenorphine-prescribing providers, however, is not uniform across geographic settings. For example, compared to urban settings, there are fewer buprenorphine prescribers in rural settings, the distance patients must travel to receive OUD treatment is substantial, and providers generally lack addiction specialty training [21, 22•].

PCP Role and Training

A recent study was conducted to help to characterize PCP ($n = 1010$) perspectives on the prescription opioid epidemic. PCPs were randomly sampled from a national database, and generalization is limited by low sampling rate (29%) and selection bias. Over half (56%) of PCPs believe that opioids are effective therapy for chronic pain while only 13% had prescribed medications for OUD [3]. More than two-thirds of PCPs (69%) in the study believed that people with OUD could be successfully treated and return to productive lives, and more than half (58%) believed that effective medications to treat OUD existed. Gaps in PCP knowledge about factors contributing to the current public health crisis were uncovered, with only 13% knowing that relatives or friends were the main sources of misused pills [23]. Fortunately, most PCPs recognized their role in helping to address OUD (83%) and were open to interventions to facilitate that [3, 23]. Efforts to engage and prepare PCPs to address OUD are increasingly important given growing data demonstrating that patients benefit when they are initiated on medications for OUD (MOUD) during acute care (i.e., emergency department and hospitalization) and prior to release from incarceration with linkage to primary care for ongoing treatment. Such data have prompted nationwide implementation efforts in diverse settings [24, 25••, 26, 27]. In parallel, there are efforts to increase the workforce capacity to address OUD as PCP training in addiction medicine remains low, and most primary care-based residency programs have yet to implement rigorous addiction-based curricula into their resident education [28, 29••]. Holt et al. demonstrated the feasibility of incorporating office-based opioid treatment (OBOT) into the context of a primary care resident run clinic [30]. Satisfaction scores among patients and residents were high, and 94% of patients reported the clinic probably or definitely helped them cope with their substance use [30]. In addition to workforce training needs, the importance of training individuals across disciplines to use and promote patient-centered, non-stigmatizing, person-first language (e.g., “person with opioid use disorder”) cannot be overstated [31].

Screening and Diagnosis

Despite the increasing prevalence of OUD and associated morbidity and mortality in the USA, it remains an underdiagnosed condition [32]. As primary care is the main

point of contact with the health system for most patients, primary care clinics are a logical location for screening to occur. The United States Preventive Service Task Force (USPSTF) in 2019 issued a draft statement recommending screening for illicit drug use in patients aged 18 and older when appropriate follow-up care can be offered [33]. The frequency of screening is not well defined, and the draft guideline defers to recommendations from SAMHSA which recommends at least yearly screening, and any time PCPs are concerned about risk of illicit drug use [34]. Interviewer-administered tools and self-administered tools appear to have similar accuracy, and each practice should determine their screening work flow and management steps for follow-up [33, 35]. Despite this, one study found that compared to screening and treatment of depression, PCPs are less likely to screen and treat OUD [36]. Within the same sample, providers felt less prepared and less confident in the treatment of OUD [36]. Other factors contributing to under screening and under diagnosis include physician time limitations, low physician preparedness, physician skepticism about the management of OUD, perceived patient resistance, and discomfort with discussing substance use [32, 33].

Screening tools used in primary care often screen for a range of substance use, and their utility depends both on the accuracy of the tool and the speed at which it can be performed. Examples include the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST), the Drug Abuse Screening Test (DAST-10 or DAST-20), the Single Item Drug Screener, and the CAGE-AID (cut down, annoyed, guilt, eye opener, adapted to include drugs). More recent screening tools evaluated in the primary care literature include the Screening of Drug Use (SoDU) and the Tobacco, Alcohol, Prescription Medications, and Other Substance Use (TAPS) [32, 37]. The SoDU is a two-question screening tool that has been recently validated in a Veteran Affairs primary care setting and found to have 100% sensitivity and 86.3% specificity for detecting OUD [37]. TAPS screening tool consists of two parts. TAPS 1 is a four-question screening tool that can be followed by TAPS 2, a brief assessment survey. It is self or provider administered and has also been validated in a primary care setting [38, 39]. The tool is easy to use, though sensitivity for detecting substance use disorders in the validation sample was low (48–74%), particularly for prescription OUD (48%) [39]. A follow-up study of the TAPS 1 as a stand-alone tool in primary care showed improved sensitivity for detecting problem illicit drug (91%) and prescription medication (85%) use and illicit (93%) and prescription medication (89%) substance use disorder [38]. Since brief screening tools often do not indicate the specific drug used or the extent of the drug use, all positive screens should be followed up to determine the type and severity of the underlying substance disorder using the Diagnostic and Statistical Manual (DSM)-5 diagnostic criteria. Once OUD is identified, it is important to screen for

other substance use and comorbid conditions that may contribute to OUD and impact treatment response. For example, non-opioid substance use is prevalent among patients with OUD, most often alcohol and tobacco use, and contributes to long-term harms and risk of overdose [17].

Management Strategies

Like the management of other chronic diseases, most patients with OUD are suitable for treatment in the primary care office with a stepped care approach whereby patients may be referred to specialty care as needed. In fact, the management of OUD in primary care has been shown to improve adherence to MOUD and increase patient satisfaction, as discussed below [7]. Indications to step up care to a more structured treatment setting and/or a provider with specialty training in addiction medicine may include failure to reach treatment goals, polysubstance use, patients on other sedating medications (i.e., benzodiazepines), severe psychiatric comorbidity, or severe cardiopulmonary disease.

MOUD is the gold standard treatment for OUD [6, 7, 35, 40, 41]. In the USA, the MOUD available in the primary care office is buprenorphine with or without naloxone and injectable naltrexone (Box 1). Buprenorphine has consistently been demonstrated to decrease opioid use and increase treatment

Box 1 Medications for opioid use disorder treatment in primary care in the USA

Opioid agonist medication

Buprenorphine is currently the only opioid agonist used in office-based opioid treatment (OBOT) in the USA. Buprenorphine is a semisynthetic partial agonist with very high affinity at the opioid μ receptor. As a partial agonist, there is a ceiling effect on respiratory depression; however, the risk of overdose increases when combined with other respiratory depressants. For the treatment of opioid use disorder (OUD), the most commonly used formulation is buprenorphine—naloxone. It is available as a dissolvable sublingual tablet or film. Buprenorphine mono-product is available as a sublingual tablet, and more recently as an implant or extended release subcutaneous injection. Common adverse effects include constipation and headache; transaminases may become elevated in patients with chronic hepatitis C or alcohol use. Buprenorphine is safe for patient with decreased renal function. It is primarily metabolized in the liver, so administration to patients with severe liver impairment requires close monitoring.

Opioid antagonist medication

Naltrexone is an opioid μ receptor antagonist with a high binding affinity and long half-life. It prevents the analgesic and euphoric effects of opioids. Importantly, if naltrexone is administered to a patient before sufficient time has elapsed from their last opioid use, the naltrexone may abruptly precipitate withdrawal. Naltrexone is available in 2 formulations: oral (50 mg taken once daily) and intramuscular (380 mg monthly). Common adverse effects of both forms include nausea, which typically resolves after a few days of use, and hepatotoxicity, which is rare; in addition, with the intramuscular form, an idiosyncratic injection site reaction may occur, lasting for several weeks.

retention, resulting in improved health (i.e., decreased HCV and HIV acquisition) and survival [6, 7, 42, 43, 44••]. The addition of brief psychosocial interventions to MOUD, in the form of counseling or motivational interviewing, leads to improved treatment retention [6, 7]. A recent study highlighted that while most PCPs are aware of this, less than half (49%) provided the counseling or psychosocial intervention themselves [45]. Cognitive behavioral therapy (CBT) in addition to buprenorphine may lead to better abstinence outcomes for patients with primarily prescription opioid use, though further studies are needed to confirm this finding [46]. Older studies highlight potential benefit from adding contingency management to MOUD; however, there is no recent data to support this practice [47]. Importantly, compared to brief counseling, more extensive behavioral interventions have not been shown to significantly improve outcomes among patients receiving treatment for OUD in primary care [47, 48].

There are several challenges to implementing OUD treatment in primary care. These include provider factors (low provider knowledge, stigma), patient factors (housing insecurity, comorbid mental health disease), and systems factors (insufficient number of providers, under resourced clinics, slow uptake of evidence-based strategies for addiction care, and payment issues) [49–51]. Models of PCP-based care are evolving to address many of these issues, and some have been evaluated in the literature, though there is no good data supporting one model of care over another. The system that works best locally will depend on community and practice characteristics, funding, and clinical resource availability. Most successful models of care contain four key elements: medication management, psychosocial intervention, integration of care, and education and outreach [52••]. A recent review noted that coordinated, multidisciplinary models to support providers of MOUD lead to higher patient retention [53]. Low-barrier treatment that focuses on rapid initiation for high-risk populations, such as patients experiencing homelessness, attempt to augment patient autonomy while removing or lowering traditional barriers to OUD care, such as access, cost, and frequent appointments [51]. The observed benefits have been increased patient engagement and retention in care [54].

OBOT is the foundation of primary care-driven OUD treatment. Providers (including physicians, nurse practitioners, and physician assistants) waived to prescribe buprenorphine treat patients with OUD as part of their primary care practice [52••]. Brief psychosocial services may be delivered by the provider or referred out. Provider support in this model varies and may include a nurse coordinator and external support through existing mentoring programs, such as the SAMHSA-funded Provider Clinical Support System (PCSS). Variations in the structure of OBOT address issues of practice resource allocation, payment methods, and provider support. They leverage community resources and peer support

specialists to increase access and improve delivery of care [51]. In their 2016 scoping review, Korthis et al. review in detail many of the existing models of delivering OBOT (see Table 1) [52••].

Monitoring for medication adherence and diversion are important aspects of OBOT. While diversion of medications is unique to treatment with controlled substances, medication non-adherence is a common challenge to all chronic medical conditions managed by PCPs. Worldwide, the adherence to chronic disease treatments is low, at best 50% according to a World Health Organization report [55]. There is limited research to understand patterns of non-adherence and diversion among persons who are prescribed buprenorphine. An early study that used Medication Event Monitoring System (MEMS) to monitor adherence demonstrated that on average patients took 71% of their medication doses [56]. A qualitative study that explored perceived reasons for buprenorphine non-adherence among patients and providers showed a wide variety of influences including social and structural barriers such as transportation as well as consciously deciding to miss doses to use illicit opioids and also simply forgetting doses [57•].

Most clinical strategies for monitoring adherence and safeguarding against diversion include drug testing body fluids (urine or saliva) to ensure that buprenorphine is detected. High levels of buprenorphine and discordant ratios of buprenorphine to norbuprenorphine in the urine were found to be an important indicators of urine adulteration in a recent OBOT-based study [58]. Specifically, the study found that urine samples with norbuprenorphine: buprenorphine ≥ 0.26 are very unlikely to be adulterated (sensitivity 100%, specificity 58%), while urine buprenorphine ≥ 700 is 85% specific for urine adulteration. Importantly, the American Society of Addiction Medicine (ASAM) recommends that “drug testing should be used as a tool for supporting recovery rather than exacting punishment” [59]. While confirming the presence of buprenorphine is one of the primary reasons for performing urine/saliva testing as opposed to detecting ongoing illicit substance use, testing also allows for monitoring of other ongoing substance use and facilitates conversations about patient treatment goals and the effectiveness of the current treatment plan [59, 60]. The significance of a trusting provider patient relationship is highlighted by the fact that patients who are earlier in treatment are more likely to have a positive cocaine or opioid urine drug test result, but not report use to the provider. The likelihood of disclosure to PCPs of illicit opioid and cocaine use increases with time in treatment [61]. An alternative to monitoring adherence through testing of body fluids is to require confirmation of adherence through direct-observed therapy, either face-to-face or via video. A number of studies to date have demonstrated the feasibility of video confirmation of buprenorphine ingestion through mobile health platforms [62, 63].

Table 1 Selected models of office-based opioid treatment (OBOT)

Group-based opioid treatment (GBOT)	Care may be delivered through shared medical appointments in which medications are prescribed concurrently with group-based counseling or through group psychotherapy with medications prescribed during separate individual-based appointments [128]. While there are only a few studies looking at the benefits of GBOT, some reported benefits include increased access to care, decreased relapse rates and craving, increased retention rates, and improvement in depression and anxiety [128–130].
Massachusetts model	A nurse care manager (NCM) trained in addiction medicine plays the central role in initial assessment, medication induction, and continued patient support with physician availability and support services built around the NCM [49].
Collaborative care model (CCM)	Built on the foundation of the chronic care model which seeks to improve the delivery and practice of chronic disease management through implementation of specific evidence-based elements of care [8, 131]. In the CCM, mental health providers are integrated into the primary care setting. In one study, the CCM increased engagement in brief psychotherapy treatment plus medication use for opioid and alcohol use disorder, and patients were more likely to be abstinent from opioids or alcohol at 6 months [8].
Medical home model	Provides federal funding to support state Medicaid programs that deliver OBOT meeting specific criteria to improve care coordination, integrate primary care and behavioral services, and address social determinants of health [52•, 132].
Hub and spoke model (HSM)	Patients are assigned to one of two levels of care based on severity of illness. The hub is an opioid treatment program (OTP) for patients with more severe OUD, while spokes are primary care practices that offer OBOT for more mild cases of OUD. Psychosocial services are integrated into the delivery at the spoke [52••]. A study of the HSM looking at self-report data showed significant improvements in abstinence from opioids, reduction in use and overdose, decrease contact with emergency departments and policy, improved relations with family, and improved life satisfaction for those involved in care [133].

Addressing Viral Infections Associated with OUD: HCV and HIV

Integrating care for OUD with primary care provides a unique opportunity to simultaneously prevent and treat infections associated with OUD. With the rising prevalence of OUD, there has been a parallel increase in morbidity from hepatitis C virus (HCV) and HIV infections. After decades of decline, the incidence of HCV has been increasing [64], particularly among young adults and in rural settings [65]. In addition, while 9% of incident HIV cases in 2017 were attributed to injection drug use, recent outbreaks of HIV associated with injecting heroin and prescription opioids have additionally been reported in multiple sites around the country [66–68]. Treatment of OUD in office settings plays an important role in preventing spread of HCV [69–71] and HIV [72–74], as well as helping patients access screening and care for these viral infections.

In the USA, the current primary mode of transmission of HCV is through injection drug use [75]. Although the overall prevalence of HCV among US adults is just under 1% [76], the prevalence among persons who inject drugs is estimated to be 55% [77]. Addiction treatment settings are enriched for persons with HCV: studies suggest that a third to nearly a half of patients who receive buprenorphine in office-based and primary care settings screen positive for HCV [78, 79], while the prevalence of HCV has historically been even higher in methadone-treated samples [80–82]. Given the advent of highly efficacious and tolerable direct-acting antiviral (DAA) therapies for HCV, there is a global effort to eliminate HCV by 2030 [83]. A key strategy in that effort is the screening and treatment of HCV among persons with OUD, as well as the provision of MOUD to prevent further transmission and reinfection of HCV [84]. Current recommendations from the Centers for Disease Control and Prevention (CDC), American Association for the Study of Liver Disease (AASLD), and Infectious Diseases Society of America (IDSA) are for one-time, routine, opt-out testing for HCV and HIV for all adults,

and for annual screening for any patient who injects drugs. Historically, on-site screening for HCV at opioid treatment programs has not been offered [85]. Offering buprenorphine in office-based and primary care settings may increase HCV screening rates: a recent study of Seattle-area persons using opioids who injected drugs found that the majority (96%) who had been treated with buprenorphine in the past year reported having been screened for HCV [86].

In the DAA era, the vast majority (> 90%) of persons with HCV can be cured, and studies to date demonstrate similar cure rates among patients with treated OUD on buprenorphine [87–89]. However, persons with substance use disorders have historically faced many barriers to HCV treatment, even when engaged in addiction treatment [90]. Even in the DAA era, a 2016 study showed that among 700 OBOT patients at least a third had documented chronic HCV infection but only 2% initiated treatment [79]. However, retention in buprenorphine treatment has been shown to increase the rates of completing referrals, evaluations, and initiation HCV treatment [91•]. Qualitative studies support the indirect benefits on substance use and overall health that patients experience when they concurrently receive treatment for comorbidities like HCV and HIV with OUD treatment. One of the most common responses was notably a decrease in internalized shame and stigma [92].

Similarly, a recent systematic review documented the benefits of integrating HIV- and OUD-related care to improve rates of HIV diagnosis, HIV-related care, and decrease opioid use [93••]. An important consideration is promoting HIV prevention among patients with OUD. Despite guidelines recommending pre-exposure prophylaxis for PWID [94], general internists report relatively low willingness to prescribe PrEP to this population [95] and uptake remains unacceptably low [96]. To improve HIV prevention among people with OUD, efforts that address patient, provider, and structural level barriers will likely be needed [97]. Adding primary care services to existing mental health clinics has also been described to address comorbid OUD complications such as HIV and hepatitis C [52••].

Overdose and Suicide Prevention

While buprenorphine treatment significantly decreases mortality, the rate of death among patients in treatment is still above the general population. Thus, strategies to prevent overdose among patients in OBOT are important elements of care. Patients who are treated for OUD in primary care office-based settings should be provided with overdose prevention education and naloxone for overdose reversal [98]. A growing body of evidence starting from the mid-1990s shows that take-home naloxone kits do decrease overdose mortality among patients who use opioids. There is also evidence from a recent systematic review that acceptability and feasibility of prescribing naloxone in general primary care settings for patients on prescribed opioids is increasing [98–100]. However, there is less literature on naloxone-prescribing practices specifically within OBOT programs.

The risk of overdose for patients taking opioid agonists, including buprenorphine, is increased with concomitant use of other sedatives, including alcohol and benzodiazepines. Initial recommendations generally advised providers against prescribing buprenorphine to patients who regularly use benzodiazepines; however, the clinical approach has evolved more recently [101]. Guidelines have been updated to reflect the knowledge that patients with OUD frequently also use benzodiazepines, and that this group is at higher risk of poor outcomes if their OUD goes untreated. Thus, even in the presence of ongoing benzodiazepine use, patients with OUD should not be denied appropriate OUD treatment [102]. Estimates of prevalence of prescribed benzodiazepines among patients treated in outpatient buprenorphine settings range from 8 to 38% [103–105]. Recent studies provide evidence that benzodiazepine use does not decrease retention rates in low-barrier methadone programs and that while patients maintained on buprenorphine who are also taking benzodiazepines have an increased risk of overdose, they are also less likely to discontinue buprenorphine treatment [106, 107].

Hidden in the overdose epidemic is a growing recognition that death among patients with OUD is too often by suicide. Efforts to understand the optimal strategies to identify and address such risks are underway and have recently been comprehensively reviewed [108••].

Optimizing OUD Treatment Outcomes in Primary Care

Several factors may influence outcomes in OBOT. Patients perceive that strong relationships with their provider, a patient-centered approach to care, a safe environment accepting of self-disclosure, and effective communication between the medical care team as helping them to reach their treatment goals [109]. Longer duration of care is also associated with better outcomes, and buprenorphine should be continued as long as there is benefit, potentially indefinitely [35••,

110]. Multiple studies show relapse rates as high as 90% after leaving treatment [105, 111, 112].

The primary outcomes studied in the literature on OBOT include impacts on mortality, retention in care, and rates of relapse. There is a growing body of research demonstrating significantly decreased all-cause mortality when patients with OUD are treated with buprenorphine [43, 113–118]. However, treatment retention is a major challenge that stands in the way of achieving optimal treatment outcomes, and studies suggest rates are lower for patients on buprenorphine compared to methadone [117–121]. Although studies vary slightly in their estimates, it appears that on average, about one-half of patients treated with buprenorphine in office-based settings will continue to be retained in treatment at 6–12 months, though this may be lower for low-barrier programs [122]. The trade-off for low-barrier programs is increasing access for the highest risk populations. Low-barrier clinics that provide more flexible, “drop-in” hours hold promise for keeping the most vulnerable patients retained [123]. Certain populations have shown higher retention rates including a large VA study with retention of 61% at 1 year [124]. A number of studies have been conducted to understand the barriers to retention. Patient level factors associated with increased non-retention have included male gender, younger age, and ethnicity identified as African American or Hispanic. Current methamphetamine use [125], hepatitis C infection, unemployment, and recent injection drug use are also associated with lower retention rates. One study looking specifically at psychoactive medications (including antidepressants, benzodiazepines, and gabapentin) in an OBOT setting did not show a decrease in retention for patients on these medications [126]. Prior experience with buprenorphine tends to be a protective factor [105].

Studies looking at clinic level factors and interventions associated with retention are limited. The highest risk of treatment disengagement is in the first 4 weeks of care, and patients prescribed buprenorphine may cycle in and out of treatment. Patients who remain in treatment for over 4 weeks tend to stay engaged for

Table 2 Key areas for future research

Prevention of opioid use disorder
Retention in treatment (identifying barriers, vulnerable sub-populations, etc.)
Role for technology (mHealth, Telehealth, etc.)
Long-term MOUD in older patients (duration of treatment, transitions to different medications and care delivery settings, palliative care, etc.)
MOUD in patients with severe comorbidities (risky comorbidities and medications, pain management, etc.)
Addressing stigma associated with addiction (provider stigma/discrimination, patients' internalized stigma/shame, overlapping stigma of HIV/HCV, etc.)
Evolving collaborative/interdisciplinary models of care (achieving integrated care, models that improve adherence/retention, individualized treatment for patients, patient-centered care, etc.)

significant lengths of time, many for over a year [127]. Provider decisions, such as discharges for continued illicit substance use, undoubtedly have played a role in non-retention. However, as programs are increasingly moving toward more streamlined processes for providing access to medication and are adopting “harm-reduction” policies that are more accepting of continued substance use, these factors should be less influential.

Conclusion

With the expansion of buprenorphine into primary care, significant progress has been made over the past two decades to increase access to treatment of OUD; nevertheless, a significant treatment gap remains. To narrow the treatment gap, PCPs need to recognize and embrace their critical role in identifying and delivering evidence-based treatment to address OUD in a patient-centered manner. In addition, future research is needed in multiple domains (Table 2). First, we need longitudinal studies to understand the long-term impact of different types of MOUD on medical and psychiatric comorbidities, particularly as patients age. Second, given the life-saving benefits of buprenorphine, novel interventions (e.g., technology-based approaches) and treatment (e.g., long-acting buprenorphine formulations) approaches to promote retention, prevention of return to substance use, and re-engagement in care are needed. Third, studies to further disentangle the links between health behaviors, comorbidities, and OUD and its associated treatment are needed. Fourth, given persistent and pervasive stigmatizing beliefs regarding OUD in community and healthcare settings, multipronged approaches including education, need to be prioritized. Lastly, ongoing efforts to foster collaborations across settings (e.g., community and clinical; acute care and primary care) and disciplines (e.g., PCPs and psychiatrists) to enhance the number of patients receiving life-saving buprenorphine are urgently needed to curb the public health impact of the opioid epidemic.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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