Treatment of opioid use disorder in primary care

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ABSTRACT

Opioid use disorder (OUD) is a common, treatable chronic disease that can be effectively managed in primary care settings. Untreated OUD is associated with considerable morbidity and mortality, notably, overdose, infectious complications of injecting drug use, and profoundly diminished quality of life. Withdrawal management and medication tapers are ineffective and are associated with increased rates of relapse and death. Pharmacotherapy is the evidence based mainstay of OUD treatment, and many studies support its integration into primary care settings. Evidence is strongest for the opioid agonists buprenorphine and methadone, which randomized controlled trials have shown to decrease illicit opioid use and mortality. Discontinuation of opioid agonist therapy is associated with increased rates of relapse and mortality. Less evidence is available for the opioid antagonist extended release naltrexone, with a meta-analysis of randomized controlled trials showing decreased illicit opioid use but no effect on mortality. Treating OUD in primary care settings is cost effective, improves outcomes for both OUD and other medical comorbidities, and is highly acceptable to patients. Evidence on whether behavioral interventions improve outcomes for patients receiving pharmacotherapy is mixed, with guidelines promoting voluntary engagement in psychosocial supports, including counseling. Further work is needed to promote the integration of OUD treatment into primary care and to overcome regulatory barriers to integrating methadone into primary care treatment in the US.

Introduction

Opioid use disorder (OUD) is a common problem that contributes to morbidity and mortality worldwide.[1 2] Moreover, many people with OUD use needles to administer the drug, leading to infectious complications including HIV and hepatitis B and C.[3] Over the past few decades, the United States has seen a rise in the prescribing of opioids and, with it, a rise in non-medical use of prescription opioids (taking opioids for purposes or in a manner other than intended by the prescriber), OUD, and opioid overdose.[4] Although the opioid overdose epidemic began with an increase in mortality related to prescription opioids, with tightening of access to those it shifted to heroin in 2010 and then synthetic opioids such as fentanyl since 2013. This review is aimed at clinicians caring for patients with OUD and researchers interested in advances in treatment.

Deaths in the US due to opioid overdose have increased sevenfold from 2000 to 2015, leading to a decrease in life expectancy.[5] Recent increases in deaths due to opioid overdose in the US have been primarily driven by illicit fentanyl use.[6] The covid-19 pandemic has led to an increase in deaths due to overdose in 2020,[7] adding urgency to the need for screening and treatment in primary care settings.

As with other chronic medical conditions, primary care clinicians are on the front line of identifying and treating people with OUD. Moreover, the need for OUD treatment in the US exceeds the capacity of specialty programs.[8] Substance use disorders (SUD) have traditionally been treated in specialized programs separate from other healthcare, but an increasing move toward the integration of SUD treatment into primary care is supported by evidence.[9] SUDs have much in common with other chronic medical conditions treated in a primary care setting; for example, type 2 diabetes, like SUD, is the consequence of a complex interplay of genetics, environment, physiology, and behavior. In addition to decreasing OUD related morbidity and mortality, providing buprenorphine for OUD in a primary care setting improves the care and outcomes of other chronic medical conditions, particularly HIV and hepatitis C virus (HCV).[10-12]

The segregation of OUD in the US into federally regulated opioid treatment programs separates care from other medical treatment, perpetuates the stigma associated with this condition, and is a barrier to getting treatment. In particular, receiving treatment at sites that only treat patients with OUD, such as opioid treatment programs, explicitly identifies a

patient as having OUD and prevents anonymity. Patients report increased satisfaction with OUD treatment in a primary care setting due to the flexibility, privacy, and accessibility of treatment.[13]

Epidemiology

An estimated 26.8 million people had OUD globally in 2016, a 47.3% increase from 1990, with the highest prevalence in high income North America, followed by North Africa and the Middle East.[14] According to the 2018 National Survey on Drug Use and Health (NSDUH),[15] an estimated 808 000 Americans (0.3% of those aged 12 or older) used heroin in the previous year, more than double the 373 000 in 2007. The non-medical use of prescription opioids rose in the two decades after 1990 but has gradually declined since then: 0.6 million Americans used these agents for the first time in 1990, rising to 2.4 million in 2001 and declining to 1.9 million in 2018. Nevertheless, non-medical use of prescription opioids remains an important problem, with 9.9 million (3.7%) Americans in 2018 reporting such use in the previous year. An estimated 526 000 (0.2%) Americans met criteria for heroin use disorder; this is more than twice the number in 2002 (214 000). Moreover, an estimated 1.7 million (0.6%) met criteria for prescription OUD.

Racial disparities

Since the rise in illicitly manufactured fentanyl and other synthetic opioids in 2013, rates of fatal opioid overdose have increased at higher rates among black Americans.[16] Despite this, black Americans are less likely than white Americans to receive buprenorphine. In a retrospective cohort study of 205 405 outpatient visits between 2012 and 2015, black patients had significantly lower odds of receiving buprenorphine prescription at their visits (adjusted odds ratio 0.23, 95% confidence interval 0.13 to 0.44).[17] In this study, rates of buprenorphine prescribing were higher for self-pay and privately insured patients compared with Medicaid/Medicare coverage; however, racial disparities still existed after adjustment for insurance status. More work is needed to decrease racial disparities in who receives treatment for OUD.

Sources and selection criteria

We identified sources through a search of PubMed from 2000 to March 2020 for MeSH terms including "primary health care" and any of the following terms: "opioid-related disorders", "buprenorphine", "methadone", or "naltrexone". After reviewing the resultant 675 titles, we discarded those that were clearly irrelevant, reviewed the abstracts of the remaining papers, and included those we considered relevant. We prioritized systematic reviews and randomized controlled trials (RCTs). For areas with a lower quality of evidence, we included retrospective and observational analyses. We excluded case reports and case series. We also reviewed the reference lists of relevant review articles and reviewed and included papers if appropriate. We included only English language articles.

Screening for OUD

Screening tools

Several methods for screening for unhealthy drug use exist, one of the simplest of which is to ask the following two questions:

1. How many days in the past 12 months have you used drugs other than alcohol? (seven or more is positive)
2. How many days in the past 12 months have you used drugs more than you meant to? (two or more is positive).

In a study of more than 1200 primary care patients, these two questions were found to be more than 90% sensitive and specific for drug use disorder.[18] A positive screen should prompt further questioning about the frequency, quantity, and impact of drug use.

Tools are also available to screen for OUD among people who received prescribed opioids. One of these is the Current Opioid Misuse Measure,[19] which, in a study of 86 patients with chronic pain receiving opioids, had a sensitivity of 77% and specificity of 68% with an area under the receiver operating curve of 0.81. Another is the Prescription Opioid Misuse Index, which, in a study of 137 people in a variety of settings, had a sensitivity of 82% and specificity of 92% with an area under the receiver operating curve of 0.89.[20]

Testing urine for drugs is another way of identifying people who are taking illicit or non-prescribed opioids, but this should not be used as a screening tool. In a population with a low pretest probability of OUD, many (if not most) positive results will be false positives. Moreover, these tests do not distinguish between occasional users and people with OUD.[21] These tests are probably best reserved for monitoring patients receiving treatment for OUD and those who have a prescription for opioids (and other controlled substances), and this should not be done without a clear context and informed consent of the patient.

Guidelines

In 2020 the United States Preventive Services Task Force recommended screening for unhealthy drug use in adults age 18 or older, "when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred."[22] However, the accompanying evidence report acknowledged that "evidence of effectiveness remains primarily derived from trials conducted in treatment-seeking populations."[23]

Diagnosis of OUD

Opioid use disorder is characterized by loss of control over the use of opioids resulting in physical, psychological, and social harms. *The Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) provides diagnostic criteria for OUD, which are the same for all substances and based on the

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presence of at least two of 11 criteria, which can be divided into four clusters[24]:

I. *Impaired control*: use in larger amounts or over a longer period of time than intended; persistent desire to cut down or multiple unsuccessful attempts at cutting down or stopping use; great deal of time spent using substance or recovering from its effects; intense desire to use or craving for the substance.
II. *Social impairment*: substance use resulting in failure to fulfil obligations at work, school, or home; substance use causing or exacerbating interpersonal problems; important social, occupational, or recreational activities given up or reduced owing to substance use.
III. *Risky use*: recurrent use of substance in physically hazardous situations; continued use despite negative physical or psychological consequences.
IV. *Pharmacologic dependence*: tolerance to the effects of the substance; withdrawal symptoms with cessation of substance use.

An important caveat is that "symptoms of tolerance and withdrawal occurring during appropriate medical treatment with prescribed medications (e.g., opioid analgesics, sedatives, stimulants) are specifically not counted when diagnosing a substance use disorder."[24 25]

Treatment

Brief interventions

The implementation of brief interventions for substance use has received much attention in recent years, often as part of screening, brief interventions, and referral to treatment (SBIRT). Early studies showed brief interventions to be effective at reducing alcohol use among people with risky (but not dependent) alcohol use in primary care settings.[26] Similarly, a 2005 study of a brief intervention delivered by peer educators in a primary care setting reported reductions in heroin and cocaine use after six months.[27] However, subsequent studies have failed to show a significant effect.[28 29] These interventions seem to be most effective for people with low risk use.[30] Counseling delivered by primary care clinicians over many visits for patients with whom they have a longitudinal relationship may have a larger effect, but research is needed to demonstrate this.

Psychosocial treatment

Several psychosocial treatments can help people with OUD, including self-help groups,[31] counseling (individual or group),[25] and residential treatment.[32] Although these are typically delivered outside of the primary care setting, clinicians can help to facilitate linkage to these treatments for patients who are interested. The evidence supporting these interventions, either alone or in combination with pharmacotherapy, is limited and the effect is generally much lower than that observed with pharmacotherapy alone. Most of the recent research on these interventions is on their use in conjunction with pharmacotherapy.

Pharmacotherapy

Medically supervised withdrawal

Medically supervised withdrawal, or using medications to rapidly wean patients from opioids, is not recommended owing to increased risk of relapse and overdose after treatment of withdrawal. Most patients return to opioid use shortly after withdrawal treatment is complete, even when engaged in abstinence based treatment.[33 34] For patients who decline pharmacotherapy, opioid withdrawal can be managed safely by primary care clinicians over several days to one week; protocols studied in primary care settings include clonidine, clonidine/naltrexone,[35 36] and sublingual buprenorphine.[37 38]

Long term (maintenance) pharmacotherapy remains the first line treatment for patients with OUD,[39] and many patients presenting for opioid withdrawal management prefer long term pharmacotherapy.[34 40] In the remainder of this section, we will discuss evidence for the three drugs approved for treatment of OUD: buprenorphine, methadone, and extended release naltrexone. Table 1 summarizes dosing and outcomes for each drug.

Opioid agonist treatment

Long term pharmacotherapy is the mainstay of treatment for opioid use disorder, with the best evidence for the long acting full opioid agonist methadone and partial opioid agonist buprenorphine.[41 42] Both are on the World Health Organization's list of essential medications.[43] A 2017 systematic review of 19 cohort studies including more than 120 000 patients treated with methadone and 15 000 treated with buprenorphine found substantial decreases in all cause mortality for patients receiving opioid agonist therapy compared with those out of treatment: 11.3 and 36.1 per 1000 person years in and out of methadone treatment (unadjusted outcome in rate ratio 3.20, 95% confidence interval 2.65 to 3.86); 4.3 and 9.5 per 1000 person years in and out of buprenorphine treatment (2.20, 1.34 to 3.61).[44] A UK cohort study of 11 033 patients receiving opioid agonist treatment in primary care settings found similar reductions in all cause mortality and mortality due to drug related poisoning. The lowest risk period was from four weeks on treatment until treatment cessation (0.98 and 0.29 per 100 person years all cause and drug related poisoning mortality, respectively), compared with an adjusted mortality incidence rate ratio of 3.25 (95% confidence ratio 2.35 to 4.49) during the first four weeks of treatment, 10.37 (8.33 to 12.91) during the first four weeks after discontinuation of treatment, and 2.81 (2.28 to 3.46) more than four weeks off treatment.[45] Termination of pharmacotherapy is associated with high mortality rates in multiple large cohort studies, with a particularly high risk immediately after discontinuation of treatment.[45-48] In the UK

general practice cohort study, the risk of mortality was eight times higher in the first four weeks after discontinuation of treatment compared with the risk after four weeks or more on treatment (adjusted mortality incidence rate ratio 8.15, 5.45 to 12.91).[45] A 2010 analysis of 5577 patients from the UK general practice cohort found adjusted mortality rates of 5.3 (95% confidence interval 4.0 to 6.8) on treatment compared with 10.9 (9.0 to 13.1) off treatment.[46] When discontinuation of opioid agonist therapy is safe is not clear, but in this analysis remaining on medication for at least a year offered some mortality benefit.

Buprenorphine

Buprenorphine is a long acting partial opioid agonist that is highly effective for treatment of OUD.[41] The Drug Addiction Treatment Act of 2000 allowed for office based treatment of OUD by US physicians, with expansion to advanced practitioners (for example, nurse practitioners, physician assistants) in 2016. In the US, physicians must complete eight hours of training and advanced practitioners 24 hours of training to prescribe buprenorphine for OUD. No additional training is required to prescribe specific formulations of buprenorphine approved for pain in the US or for treatment of OUD in many other countries.[49]

Several buprenorphine formulations are available in the US. Most are co-formulated with naloxone to discourage injection or intranasal use. Sublingual tablets are available with or without naloxone in 2 mg and 8 mg doses. Sublingual strips (brand name Suboxone) are also available, but only in combination with naloxone, in dosages of 2, 4, 8, and 12 mg of buprenorphine. A rapidly dissolving higher bioavailability tablet of buprenorphine/naloxone (brand name Zubsolv) and a buccal film (brand name Bunavail) are also available. The buprenorphine dosages for the rapidly dissolving tablet and buccal formulations are different than for the sublingual formulations; 5.4 mg of the rapidly dissolving tablet and 4.2 mg of the buccal film are roughly equivalent to 8 mg of the standard sublingual tablet or film.

Evidence supports use of a daily buprenorphine dose of 16 mg or higher for most patients. In a Cochrane systematic review of 31 studies including 5430 patients, dosing of 16 mg sublingual buprenorphine daily was non-inferior to methadone.[41] A 2010 systematic review and a clinical trial published in 2013 found that higher sublingual buprenorphine doses (up to 32 mg/day) were associated with better treatment outcomes.[50 51] Some programs limit dosing of buprenorphine owing to pharmacologic studies. In one study, doses above 8 mg/day provided minimal additional benefit in terms of withdrawal suppression and opioid blockade,[52] but this study was conducted in only eight patients over 96 hours. On the other hand, observational studies suggest that insurer imposed limits on the dose of buprenorphine to 16 mg/day are associated with increased rates of relapse, aberrant drug tests, and decreased retention in treatment.[53 54] At a time when fentanyl and high potency opioids are available, many patients may need doses of buprenorphine above 16 mg and should be offered doses up to 32 mg daily. Patients who do not respond to doses up to 32 mg/day should be considered for methadone treatment.

Buprenorphine maintenance is more effective than short term taper (or medically supervised withdrawal)[55] and is associated with long term retention in primary care settings.[56-58] Although early guidelines recommended supervised initiation of buprenorphine, studies have shown the safety of home initiation compared with supervised initiation, with similar rates of retention and successful management of withdrawal.[59] Home initiation is now standard practice and does not require additional staffing to monitor dosing. Buprenorphine has a high binding affinity, which contributes to its safety, but it can displace other opioids and lead to "precipitated withdrawal" if it is administered too soon after use of a full agonist.[60] Precipitated withdrawal can be avoided by waiting to administer buprenorphine until the patient develops symptoms of opioid withdrawal (a sign of low receptor occupancy)— usually eight to 12 hours after heroin or short acting prescription opioids— and using a low initial dose of buprenorphine. Longer periods may be needed (up to 18-24 hours) for patients using fentanyl because of its lipophilicity. One case series successfully initiated buprenorphine in patients using fentanyl by using multiple low doses (2 mg buprenorphine) after patients showed mild to moderate withdrawal.[61] The use of "microdosing" protocols is also emerging, using successive small doses of buprenorphine to slowly displace full agonists from the opioid receptor.[62]

Traditionally, the standard of care includes monitoring adherence to buprenorphine with

Table 1 | Overview of pharmacotherapy for opioid use disorder (OUD)

Medication	Mechanism of action	Formulations for OUD treatment	Dosing	Outcomes	
				Mortality	Illicit opioid use
Buprenorphine	Partial opioid agonist	Sublingual tablet/film; weekly and monthly SC injections; implant	Sublingual: 8-32 mg daily. SC injections: Sublocade: 300 mg monthly × 2 months, followed by either 100 or 300 mg maintenance dose; Brixadi (CAM-2038, Braeburn): 8, 16, 24, and 32 mg weekly or 64, 96, and 128 mg monthly	Decreased	Decreased
Methadone	Full opioid agonist	Oral (tablet, liquid)	60-200 mg daily*	Decreased	Decreased
XR-naltrexone	Opioid antagonist	Intramuscular injection	380 mg IM once monthly	No significant effect-	Decreased

IM=intramuscular, SC=subcutaneous; XR=extended release.
*Maximum allowed dose of methadone varies, and emerging evidence suggests that patients may need higher doses than previously allowed.
-Based on limited evidence, primarily observational studies with relatively small numbers receiving naltrexone.

periodic drug testing,[63 64] although no evidence shows that drug testing improves clinical outcomes. Recent changes in regulations due to the covid-19 pandemic allowing for increased treatment via telemedicine have prompted decreased use of drug testing and re-evaluation of this practice. When used, drug testing should be used as a therapeutic tool, in a patient centered rather than punitive way. For example, a positive test for illicit opioid can prompt discussion about whether a patient needs an increase in the buprenorphine dose to suppress cravings and what triggers the patient's drug use. A positive test for non-opioid substances (such as cocaine, cannabis, and benzodiazepines) can be used to prompt further discussion on the effect of these drugs on the patient and measures that can be taken to minimize harm. In general, use of other drugs is not a reason to discontinue buprenorphine, because doing so would put the patient at risk for overdose and death.[65]

Treatment with buprenorphine in office based settings is associated with many positive outcomes, including increased primary care screening,[66] high patient satisfaction,[67] and decreased healthcare costs.[68] Good outcomes have also been shown for patients with comorbid chronic pain.[69 70] Buprenorphine treatment has been successfully integrated into diverse primary care settings, including community health centers and HIV clinics.[71-73] Patients initiated on buprenorphine in the emergency department and during inpatient hospital admissions can be successfully transitioned to ongoing treatment in primary care.[74 75] Multiple models have been developed to expand access to buprenorphine in primary care settings[76]; these are outlined in table 2. Models include collaborative care, "hub and spoke," and integration into HIV clinics. Barriers to implementing buprenorphine in primary care include lack of trained primary care clinicians, reimbursement models that do not support care coordination and psychosocial services, persistent stigma associated with pharmacotherapy for OUD, and long travel times for patients in rural areas. Current models of care use various strategies to overcome barriers, such as integrating training and education, use of non-physician clinicians, development of reimbursement models to support delivery of pharmacotherapy, use of tele-education and telemedicine, tiered care models, and engagement of stakeholders.[76]

Adjunctive services

Evidence that additional psychosocial interventions improve outcomes for patients treated with buprenorphine is limited.[88] Among eight key RCTs, four studies of additional counseling or cognitive behavioral therapy showed no additional benefit on retention or opioid negative urine drug tests.[89-92] Three RCTs that included contingency management arms showed longer periods of abstinence and higher rates of drug negative urine specimens compared with standard counseling.[93-95] However, because of resource constraints, contingency management is rarely practical in most primary care settings. Table 3 summarizes the study findings.

Other adjunctive therapies may be of benefit. In a cohort study of adding brief mindfulness training in 40 patients initiating buprenorphine for OUD, high uptake of daily mindfulness practice was associated with decreased six month relapse rate compared with low uptake groups (11% *v* 42%; P=0.033).[97] A small RCT of primary care based community health workers showed increased engagement in primary care among patients with opioid use disorder. In the study, 18 (24%) of the 75 community drug team clients in the intervention arm but none of the 80 community drug team clients in the control arm were in shared care at 12 months (χ^2=9.37; P<0.01).[98] Further research is needed to determine who would benefit from psychosocial interventions and how best to match treatment to individual needs.

Methadone

The long acting full opioid agonist methadone was first used as treatment for OUD by Dole and Nyswander in 1967.[99] It is a highly effective treatment, with a 2009 Cochrane systematic review showing its efficacy in decreasing illicit opioid use compared with no medication across six RCTs (risk ratio 0.66, 95% confidence interval 0.56 to 0.78).[42] A systematic review of 221 studies including 2279 patients found that higher doses of methadone were associated with higher retention in treatment (relative risk 1.36, 95% confidence interval 1.13 to 1.63), decreased overdose mortality (0.29, 0.02 to 5.34) and decreased illicit opioid use (1.59, 1.16 to 2.18), with best outcomes with doses of at least 60-100 mg.[100] Strong evidence of poor outcomes after discontinuation of methadone, including increased mortality, also exists.[101 102] Owing to its long half life, methadone is typically started at 30-40 mg once daily and titrated slowly until an effective dose is achieved (for example, by 5 mg every other day). Closer medical monitoring is needed than with buprenorphine owing to its long half life and the risk of respiratory depression. As the dose is increased, patients are monitored for craving, withdrawal, sedation, and respiratory depression, with the goal of reaching a dose suppressing opioid craving while avoiding over-sedation.

Methadone treatment is successfully managed by primary care clinicians in many countries. Multiple studies (both RCTs and cohort studies) have shown the efficacy of methadone treatment in primary care settings.[103-107] The ANRS Methaville study, a pragmatic multicenter RCT in 221 patients, showed non-inferiority of methadone in primary care compared with specialty settings based on rates of abstinence from illicit opioids (P=0.39) and treatment retention (P=0.47), with higher treatment engagement (P<0.001) and patient satisfaction (P=0.01) in primary care settings.[104] Additionally, an Irish national cohort study of 6983 patients found that retention in methadone treatment in primary

Table 2 | Models of primary care based buprenorphine treatment

Model	Description	Evidence	Advantages	Challenges
Primary care office based opioid treatment (OBOT)[77]	Waivered prescriber provides buprenorphine to patients as part of general primary care practice; variable on-site psychosocial services. Some practices designate clinic staff member to coordinate care	Retention in treatment similar to methadone treatment; 38-80% 1-2 year retention across multiple cohort studies[68 78-80]	Low threshold for treatment entry; patients are provided with treatment at primary care clinics where they are already engaged. No additional staffing needed (fully integrated into outpatient treatment); financed by provider reimbursement of billable visits	No funding for on-site psychosocial services; no additional support for clinicians
Integration with HIV primary care (BHIVES)[81]	HIV clinicians prescribe buprenorphine along with HIV/primary care, supported by non-physician coordinator and variable on-site psychosocial services	BHIVES cohort of 303 participants across 9 clinics: 49% 12 month retention; 50% decrease in past 30 day opioid use[82]	HIV and buprenorphine care typically covered by insurance. Patients view this model as patient centered owing to co-location of services[31]	Lack of financial support for on-site counseling in clinics without designated Ryan White Funding
Nurse case manager model[83]	Generalist clinicians work with nurse case managers for co-management of patients (nurse case manager can bill for patient management visits)	375% increase in number of buprenorphine waivered physicians within 3 years.[84] Cohort study of 408 pilot patients: 51% 1 year retention with 91% illicit opioid negative drug testing[83]	Use of skilled non-physician to offload prescribing physician burden, emphasis on provider training, and financial sustainability through Medicaid reimbursed nurse care manager visits	Variable availability of psychosocial services and nurse care managers trained in OUD pharmacotherapy. Most states lack Medicaid coverage for nurse OUD care management visits
Hub and spoke[85]	Patients triaged to 2 levels of care at intake: "spokes" are primary care clinics that prescribe buprenorphine through OBOT model; regional OTP "hubs" care for more complex patients and provide consultative services to spokes. Based on stability, patients may be transferred between hubs and spokes	No published studies on outcomes	Tiered care system; integration of primary care with regional OUD specialty expertise; embedded care coordinators and psychosocial services at spokes	May create barriers to treatment for patients who are unable or not willing to go to "hubs" for more intensive treatment. Requires OTP hub willing to partner. Funding mechanism is part of Medicaid block grant and not applicable to many US states
Project extension for community healthcare outcomes (Project ECHO)[86 87]	Primary care clinics in rural New Mexico linked with a university health system using an internet based audiovisual network for mentoring and education	After implementation, New Mexico experienced more rapid growth in buprenorphine waivered prescribers compared with other US states[87]	Feasible model to support rural providers with buprenorphine mentoring and increased screening; effective at supporting primary care providers to become waivered. Continuing medical education credits for teleconference participation	Lack of direct contact between off-site experts and patients. Limited availability of face-to-face expertise in OUD pharmacotherapy for high risk patients

BHIVES=Buprenorphine HIV Evaluation and Support Waivered prescriber; OBOT=office based opioid treatment; OTP=opioid treatment program; OUD=opioid use disorder.

care settings was associated with decreased all cause and drug related mortality (adjusted mortality rate ratios 3.64 (95% confidence interval 2.11 to 6.30) and 1.63 (0.66 to 4.00), respectively),[108] with longer retention in treatment for patients on higher doses of methadone (60-120 mg *v* <60 mg; P<0.001).[109] A US based RCT found that clinical outcome rates of opioid use by self-report and urine drug testing were similar when patients who were stable on methadone were transferred to a primary care setting compared with continuing treatment at a specialized opioid treatment program (P=0.39); moreover, patient satisfaction was significantly higher for patients treated in primary care (P=0.001).[103]

Despite this evidence, US regulations prohibit use of methadone to treat OUD outside of federally regulated opioid treatment programs,[110] preventing its use in primary care settings (although it can be prescribed for chronic pain). In 2019 approximately 408 500 Americans were receiving methadone from 1691 treatment programs.[111] Patients must go to the opioid treatment program in person to receive their methadone supply, with daily appointments needed early in treatment and a requirement for participation in psychosocial counseling. A push has been made to expand methadone treatment to US primary care settings to increase access to care. A survey of 71 primary care providers in New York City found that 33% were willing to prescribe methadone and 66% said they would if given proper training and support (88% among HIV care providers).[112] Authors estimated that if each of the willing providers treated 10-20 patients with methadone, they could serve 470-490 patients, a population the size of three to five average methadone clinics. Many primary care based models partner with community pharmacies to allow for supervised dosing of methadone; this can be a practical way to expand treatment in rural settings and was feasible in two US based pilot studies.[113 114] Additionally, patient centered methadone treatment models (where counseling is optional, patients are involved in treatment decisions, dose limits are removed, and the focus on abstinence is less) have been shown to be clinically effective and cost effective across multiple studies.[115-117] An RCT of 300 patients starting methadone compared patient centered methadone with treatment as usual and found no significant differences in treatment retention, measures of opioid use, other patient outcomes, or cost (P=0.49).[117] Patients in the patient centered methadone arm attended fewer group counseling services (P>0.05) but similar numbers of individual counseling sessions.[117] A cohort study of 217 patients attending a methadone program who transitioned to a patient centered model found no significant differences in two year treatment retention or in opioid or benzodiazepine use between cohorts initiated before, during, and after transition to patient centered treatment.[115] Although counseling became voluntary with patient centered methadone, the number of therapist visits did not change significantly between pre-transition and post-transition cohorts. The average methadone dose increased from 50.2 mg to 92.2 mg after the

Table 3 | Summary of randomized controlled trials (RCTs) on effect of adding psychosocial interventions to buprenorphine

Study	Study population	Intervention	Outcomes
Fiellin et al, 2013[90]	141 patients with opioid dependence in primary care setting	24 week RCT. Patients randomized to physician management versus physician management plus CBT. CBT arm offered weekly 50 minute CBT session for first 12 weeks of treatment. Patients attended average 6.7 (SD 3.3) of 12 possible CBT sessions	Reduction in illicit opioid use from 5.3 days/week pre-treatment to 0.4 days/week at 12 weeks (P<0.001), with no difference between CBT and physician management only groups (P=0.96); significant increase in maximum consecutive weeks of opioid abstinence over time on buprenorphine (P<0.001) but no difference between groups (P=0.84)
Ling et al, 2013[91]	202 patients with opioid dependence	After 2 week buprenorphine initiation phase, patients randomized to weekly CBT, CM, CM plus CBT, or buprenorphine alone. Participants in CM arms entered drawing for monetary rewards based on opioid negative UDTs	No differences in opioid negative urine tests or retention in treatment in intervention arms versus buprenorphine alone (x^2=1.25; P=0.75)
Weiss et al, 2011[89]	653 treatment seeking outpatients with prescription opioid dependence	2 phase RCT. Phase 1: 2 week buprenorphine stabilization, 2 week taper, and 28 week post-medication follow-up. Phase 2: extended (12 week) buprenorphine treatment, 4 week taper, and 8 week post-medication follow-up. In both phases, patients randomized to standard medical management (SMM) or SMM+opioid drug counseling	No difference in opioid use by counseling condition at end of phase 1 (P=0.36), end of phase 2 (P=0.27), or 8 week post-treatment follow-up (P=0.22). In both groups, patients were significantly more likely to abstain from opioids while on buprenorphine versus post-taper (49.2% *v* 8.6%; P<0.001)
Fiellin et al, 2006[92]	166 outpatients with opioid dependence	24 week RCT comparing standard medical management with either once weekly or thrice weekly medication dispensing or enhanced medical management and thrice weekly medication dispensing	All groups had significant decreases in illicit opioid use (P<0.001). No difference in percentage of opioid negative urines (P=0.82), maximum consecutive weeks of abstinence (P=0.54), or 24 week study retention (P=0.64) between treatment arms
Bickel et al, 2008[93]	135 outpatients with opioid dependence	23 weeksí treatment. Three arms: 1) therapist delivered CRA with vouchers; 2) computer assisted CRA with vouchers; 3) standard medical management	Therapist delivered and computer assisted CRA plus vouchers interventions produced comparable weeks of continuous opioid and cocaine abstinence (M=7.98 and 7.78, respectively) and significantly greater weeks of abstinence than standard intervention (M=4.69; P<0.05). No difference in retention (x^2=0.73; P=0.69)
Christensen et al, 2014[94]	170 outpatients with opioid dependence	12 week RCT of internet based CRA+CM (CRA+) and buprenorphine versus CM alone plus buprenorphine. CRA included thrice weekly 30 min web based modules	CRA+ group had 9.7 total days more of abstinence (P=0.011) and decreased risk of dropping out of treatment (hazard ratio 0.47, 95% CI 0.26 to 0.85)
Schottenfeld et al, 2005[95]	162 people with cocaine and opioid dependence	24 week double blind RCT. Patients randomized to methadone or buprenorphine and to CM (monetary vouchers for opioid and cocaine negative UDTs) or performance feedback (slip of paper with UDT results). In CM arms, escalating voucher values for first 12 weeks and then reduced to nominal value in weeks 13-24	People in CM groups had longer periods of abstinence and greater proportion of drug-free tests during period of escalating voucher value (P<0.05) but no significant differences over entire 24 week study (P=0.26)
Miotto et al, 2012[96]	94 outpatients with opioid use disorder	52 week study comparing buprenorphine in 3 distinct treatment settings: 1) opioid treatment program (OTP) offering individual counseling; 2) group counseling program using manualized matrix model (MMM) of CBT; 3) outpatient clinic with standard medical management	No difference in opiate negative drug tests at 9 (P=0.15) or 20 weeks (P=0.08). Decreased retention in OTP (21.4%) and primary care (33.3%) compared with MMM group (51.5%; P=0.05). Mean buprenorphine dose was significantly higher at OTP and MMM compared with primary care site (P=0.00)

CBT=cognitive-behavioral therapy; CM=contingency management; CRA=community reinforcement approach; UDT=urine drug test.

program change (which included lifting dose limits and involving patients in dosing decisions). These could provide a model for provision of methadone in primary care where on-site counseling services are not always available.

Naltrexone

The newest medication for OUD in primary care settings is the opioid antagonist naltrexone. Oral naltrexone has poor efficacy for treatment of OUD.[118] However, a once monthly intramuscular extended release formulation has been shown to be superior to placebo in a six month RCT of 250 patients, decreasing opioid cravings (P<0.001), increasing treatment retention (P=0.0042), and decreasing relapse rates (P<0.001).[119] Extended release naltrexone was superior to oral naltrexone in an RCT in which both were combined with behavioral treatment (24 week treatment retention: 57.1% *v* 28.1%; hazard ratio 2.18, 95% confidence interval 1.07 to 4.43).[118] An RCT comparing extended release naltrexone with sublingual buprenorphine in 570 participants over 24 weeks found that outcomes (opioid negative urine, opioid abstinent days) with extended release naltrexone were inferior in intention to treat analysis (P<0.0001); however, among patients who were successfully inducted, outcomes were similar in the extended release naltrexone and buprenorphine groups.[120] This was due to a significant induction hurdle for extended release naltrexone with significantly fewer patients successfully initiated on extended release naltrexone (204/283; 72%) than buprenorphine (270/287; 94%) (P<0.001).

A 2018 systematic review of 34 studies of extended release naltrexone for OUD found that the success of induction was lower in studies that included patients who needed opioid detoxification (62.6%, 95% confidence interval 54.5% to 70.0%) compared with studies that included patients already detoxified from opioids (85.0%, 78.0% to 90.1%).[121] Only 44.2% (33.1% to 55.9%) of patients took all scheduled injections of extended release naltrexone, which were usually six or fewer. To date, studies have failed to show a significant effect of extended release naltrexone on the risk of overdose and death; this may be due to the fact that observational studies have generally had small numbers of people on this treatment.[122] More longer term studies are needed, including pragmatic studies in primary care settings.

How to transition to naltrexone as an outpatient

Most studies of initiation of extended release naltrexone have been conducted in inpatient treatment settings, and more work is needed in primary care settings. Two studies (one RCT and one observational study) have shown the feasibility of a one week extended release naltrexone induction protocol in outpatient settings, using an increasing dose of oral naltrexone and adjunctive medications.[123 124] An RCT found that participants assigned to naltrexone assisted withdrawal management were significantly more likely to be successfully inducted to extended release naltrexone (56.1% *v* 32.7%; χ^2 6.37; P=0.012) and to receive the second injection at week 5 (50.0% *v* 26.9%), compared with a buprenorphine taper followed by a one week delay.[124]

Harm reduction

Harm reduction refers to measures that aim to reduce the harms associated with drug use without necessarily targeting drug use itself, such as syringe service programs, which decrease HIV and HCV transmission,[125–127] and supervised consumption sites.[128] In a broader sense, harm reduction can be used to describe treatment models that recognize that not all patients may want to abstain from drug use and aim to provide low barrier, low threshold treatment that meets patients where they are. In primary care settings, evidence based harm reduction practices include teaching safe injection practices, fentanyl test strips, prescribing naloxone to decrease fatal overdoses, and HIV prophylaxis.

Teaching safe injection practices

Educating injecting drug users on safe injection practices can help to reduce the risk of infectious complications.[129] Not sharing needles or "works" (that is, drug injection equipment), not licking needles, and cleaning works with bleach are examples of practices that decrease the risk of transmission of HIV and HCV. Behaviors that can help to decrease the risk of fatal overdose include not using drugs alone, having naloxone accessible, using less drug than usual, pushing the syringe plunger more slowly than usual ("go slow"), administering a tester shot, and snorting instead of injecting. Fentanyl test strips can be used to test drugs for presence of fentanyl, with a positive test resulting in a change to safer drug use practices to decrease the risk of overdose in one qualitative study.[130]

Naloxone distribution

The opioid antagonist naloxone is a key tool in curbing mortality due to opioid overdose and can be easily prescribed from primary care settings to both patients with OUD and affected friends and family members.[131] Prescription of naloxone with brief education is safe and effective in primary care[132]; it should be prescribed to all patients with OUD, as well as patients likely to witness an overdose (including those living in high prevalence communities or with a family member with OUD). The increase in contamination of drug supply (including cocaine and cannabis) with illicitly manufactured fentanyl in some US markets means that patients who use any street drugs may also benefit from naloxone.

HIV pre-exposure prophylaxis

In the Bangkok Tenofovir study, prescribing daily tenofovir to people with injection drug use but not infected with HIV reduced the incidence of HIV from 0.68 per 100 person years to 0.35 per 100 person years, a 49% (95% confidence interval 9.6% to 72.2%) reduction (P=0.01).[133] On the basis of this and other data, the Centers for Disease Control and Prevention (CDC) recommend HIV pre-exposure prophylaxis (PrEP) to decrease the risk of transmission among people with injecting drug use.[134]

Special populations

Pregnant women

OUD in pregnant women presents unique risks and challenges. Several retrospective and prospective cohort studies conducted over several decades and involving thousands of women have shown that pregnant women with OUD are more likely to have pre-eclampsia, miscarriage, and premature delivery, and their babies are at risk for low birth weight, admission to a neonatal intensive care unit, and prolonged treatment for neonatal abstinence syndrome (NAS).[64 135]

Pregnancy, however, can also serve as an opportunity for pregnant women to begin treatment for OUD, as they will likely have more interactions with healthcare providers and may have increased access to medical assistance during pregnancy and the postpartum period.[136] According to guidelines from the American Society of Addiction Medicine (ASAM) and American College of Obstetricians and Gynecologists, the preferred treatment options for OUD in pregnant patients are the opioid agonists methadone or buprenorphine.[64 137 138] A systematic review of 15 observational studies including 1126 pregnant women undergoing detoxification from opioids found that detoxification was associated with poor outcomes, owing to low detoxification completion rates and high rates of relapse (no P values reported owing to variability in study methods and overall low quality of evidence).[137] Data on the effect of detoxification on maternal and neonatal outcomes beyond delivery are limited, with studies reporting mixed results on severity of NAS.[137] Compared with white non-Hispanic women, black non-Hispanic and Hispanic women had a lower likelihood (odds ratio 0.37 (95% confidence interval 0.28 to 0.49) and 0.42 (0.35 to 0.52), respectively) of receiving medication for the treatment of OUD.[139]

Although methadone and buprenorphine are both efficacious treatments of OUD in pregnant women, data from RCTs and meta-analyses suggest that buprenorphine is associated with a lower risk

of preterm birth (risk ratio 0.40, 0.18 to 0.91),[139] shorter duration of neonatal withdrawal (4.1 *v* 9.9 days; P<0.003),[140] higher birth weight (RCT weighted mean difference 277 (104 to 450) g),[139] a larger head circumference (RCT weighted mean difference 0.90 (0.14 to 1.66) cm),[139] and equivalent measurements of fetal death, fetal/congenital anomalies, and other fetal growth differences compared with treatment with methadone.[139]

Women treated with buprenorphine or methadone during pregnancy should be encouraged to breastfeed their newborns. In a retrospective cohort study of 190 opioid dependent mother and infant pairs, breastfeeding was found to decrease the number of newborns who needed treatment for NAS (52.9% *v* 79.0%; P<0.001) and to decrease the length of stay in newborns with NAS (14.7 *v* 19.1 days; P=0.049).[141] Furthermore, an observational study of 48 women found that rooming-in (observing infants for signs of withdrawal while they stay in the same room with their mothers) has been shown to reduce the need for pharmacologic treatment (92% *v* 14%; P<0.001) and shorten the length of stay of newborns at risk for NAS (33 *v* 5.5 days; P<0.001).[142]

People with co-occurring psychiatric disorders

Substance use disorders are associated with psychiatric disorders; people with each are at higher risk of having the other than are people without either. Possible reasons for this association include substance use causing psychiatric disorders, people with psychiatric disorders using substances to treat symptoms, and shared risk factors for both conditions. In patients with OUD, the lifetime prevalence of comorbid psychiatric disorders has been reported to be between 24% and 86%, with mood and anxiety disorders being the most common axis I disorders and antisocial personality disorder the most frequently diagnosed axis II condition.[143-145]

In people with co-occurring disorders, determining whether they have a substance induced disorder or a primary psychiatric disorder can be difficult.[144] Many people seeking treatment for OUD report symptoms of depression and anxiety, and the general approach is to tackle their substance use first, unless an indication for urgent psychiatric intervention is present (for example, acute psychosis, risk of self-harm). Studies show that providing pharmacotherapy for OUD without any additional services can improve mood and symptoms of depression and anxiety.[146] A randomized trial of 50 people with coexisting OUD and other psychiatric symptoms who were waitlisted for comprehensive treatment showed that treatment with buprenorphine alone, without psychosocial counseling or psychotropic drugs, reduced the mood and anxiety symptoms in this group compared with a waitlist control group, as measured with the Beck Anxiety Inventory (P<0.05), Beck Depression Inventory (P<0.01), Brief Symptom Inventory (P <0.05), and psychiatric subscale of the Addiction Severity Index (P<0.05).[146]

People with other chronic medical conditions (HIV, HCV)

HIV infection— OUD can have a detrimental effect on the health and treatment of people infected with HIV. In a cohort study of 3322 patients with HIV, those with current SUD (about a third with OUD, two thirds with cocaine use disorder) were less likely to be treated with antiretroviral therapy compared with those without SUD (84.4% *v* 80.3%; P=0.004).[147] Moreover, people with SUD have been found to have decreased rates of appropriate CD4 cell monitoring (80.0% *v* 70.9%; P=0.001), appropriate pneumocystis pneumonia prophylaxis (95.0% *v* 90.1%; P=0.016), HIV viral suppression (51.9% *v* 41.4%; P<0.001), and vaccinations (pneumococcal conjugate vaccine 23 vaccination rates 89.3% *v* 84.6%; P<0.001).[147] However, multiple studies have found that treatment with methadone or buprenorphine is associated with improved HIV treatment outcomes and decreased all cause mortality.[148-150] A systematic review and meta-analysis of 32 studies found that treatment with methadone or buprenorphine enhanced patient recruitment on to antiretroviral therapy (hazard ratio 1.69, 1.32 to 2.15), adherence to antiretroviral therapy (odds ratio 2.14, 1.41 to 3.26), and HIV viral suppression (odds ratio 1.45, 1.21 to 1.73).[150]

Chronic HCV infection is common among people with OUD, especially those with a history of injecting drug use. An estimated 2.4 million Americans were infected with HCV in 2020, and the prevalence among people with injecting drug use was estimated to be 70-80%.[151] Unfortunately, many people with chronic HCV infection are never offered treatment owing to the mistaken belief that abstinence from drug use is needed for successful treatment.[152 153] However, in multiple studies, patients with active OUD, including active injecting drug use, recent opioid use, or engagement in pharmacotherapy for OUD, have treatment success rates comparable to those for non-drug using cohorts (>90% among people with OUD).[154-157] Co-treating OUD and chronic HCV infection can help to improve outcomes for both conditions. In a prospective observational study of 100 people with injecting drug use with comorbid OUD and HCV infection receiving services from a harm reduction organization drop-in center in Washington, DC, the probability of attaining sustained viral response of HCV infection at 24 weeks was higher in those receiving opioid agonist medications at week 24 (91% *v* 63% of those not receiving opioid agonist; P=0.001).[155] No significant relation to sustained viral response was found according to housing status, injecting drug use, or even interruption of treatment.[155] Furthermore, pharmacotherapy for OUD reduces the risk of acquiring HCV or being re-infected with HCV by about half.[154 158] Treatment of OUD with methadoneor buprenorphine is associated with a 60% lower risk of incident HCV infection, but only if patients report that their dosage is adequate to prevent withdrawal and craving.[158]

People with chronic pain

Chronic pain is common and associated with being treated with opioids, sometimes for extended periods of time. A minority of these people will develop OUD; rates vary depending on the population studied and the definitions used, with one review estimating rates of 8-12%.[159]

The diagnosis of OUD among patients with chronic pain who are receiving prescription opioids is complicated by the fact that these patients may be less likely to acknowledge that they have a problem because they perceive their use as therapeutic and may be fearful of being cut off from prescribed medications. As noted earlier, DSM-5 specifies that for people who are treated with opioids, tolerance and withdrawal (two of the 11 criteria) should not be used to diagnose OUD.[24]

In response to the increased prescribing of opioids for chronic pain and harms associated with this, the CDC issued guidelines in 2016, which (among other measures) limited the prescribing and dosage of opioids.[160] The guidelines led to forced tapers or discontinuation of opioids, with some reports of harm associated with this practice.[161] In a 2019 response to this, the US Department of Health and Human Services issued a guide on long term opioid dosage reduction or discontinuation, recommending a "thoughtful, deliberative, collaborative and measured" approach and against "abrupt dose reduction or discontinuation."[162]

For people with chronic pain and OUD, as with other people with OUD, opioid agonist therapy with buprenorphine or methadone is generally the best option.[163] Buprenorphine is often the easiest to access, and clinicians who are prescribing opioids for chronic pain can switch to prescribing buprenorphine when harms or concerns exist. Some authors have advocated increased use of buprenorphine as an alternative to other opioids for chronic pain, even among people who do not meet criteria for OUD.[164] Of note, some formulations of buprenorphine are specifically approved in the US for pain, and their prescription does not require a waiver.

When to refer for specialty treatment

Many people with OUD can be successfully treated by primary care clinicians, but some will need more intensive monitoring and support than can be provided in a typical primary care setting. Indications for referral to specialty treatment would include continued use of drugs or alcohol with evidence of harm and deterioration in functioning. Referral should be done in a positive and supportive manner and not as a punitive response. For example, a person with OUD who is receiving buprenorphine and continues to use illicit opioids may do better in a methadone maintenance program; the primary care clinician can help to facilitate this transition but should not simply stop prescribing buprenorphine without careful consideration of the risks to and feasibility for the patient (transportation, schedule, etc).

Guidelines

Multiple guidelines have been developed for treatment of OUD and include guidance on treatment of OUD in outpatient settings. To date, no specific guidelines for treatment of OUD in primary care settings are available, but recommendations for general OUD treatment can be applied to primary care practices. Major guidelines in the US include the ASAM National Practice Guideline for Treatment of Opioid Use Disorder,[64 165] Substance Abuse and Mental Health Services Administration Treatment Improvement Protocol 63: Medications for Opioid Use Disorder,[166] and 2018 Canadian National Guidelines.[167] The ASAM guidelines were updated in 2020 and are the most comprehensive, including sections on screening and diagnosis, both medications and psychosocial treatments, and treatment of special populations, including pregnant women.[165]

All organizations strongly recommend offering patients treatment with the opioid agonist medications buprenorphine and methadone (with extended release naltrexone considered second line), advise against opioid withdrawal treatment, and recommend referring patients to psychosocial treatment on a voluntary basis only (that is, not withholding pharmacotherapy for patients who decline or lack access to psychosocial treatment). The Canadian guidelines are unique in promoting buprenorphine over methadone as first line therapy owing to its superior safety profile.[167]

Emerging treatments

Long acting formulations including weekly and monthly injectable extended release buprenorphine have been recently developed and shown to be effective for treatment of OUD and associated with high patient satisfaction and increased quality of life measures.[168-170] Some logistical barriers exist in the US, including cost and the need to obtain the drug from specialty pharmacies. At this time, their place in the treatment continuum is unclear and more research is needed on how best to integrate these promising treatments into primary care setting.

Telemedicine is increasingly being used in primary care settings, with rapid expansion during 2020 due to the covid-19 pandemic. This is a promising area for expansion of access to care in both urban and rural settings. More research is needed for evidence based practices for treatment of OUD by telehealth.

Conclusions

Opioid use disorder is a common, treatable chronic disease that can be managed effectively in primary care settings. Untreated OUD is associated with considerable morbidity and mortality; notably, overdose and infectious complications of injecting drug use. Withdrawal management and medication tapers are not effective and are associated with increased rates of relapse and death. Treatment with pharmacotherapy is the mainstay of OUD treatment, and evidence strongly supports its integration into primary care settings. The strongest evidence is for

the opioid agonists buprenorphine and methadone, with less evidence for the opioid antagonist extended release naltrexone. Treating OUD in primary care settings is cost effective and improves medical outcomes, particularly in patients with HIV and HCV. More research is needed on the role of behavioral interventions in supporting pharmacotherapy. Further work is also needed to promote the integration of OUD treatment into primary care and to overcome regulatory barriers to integrating methadone into primary care treatment in the US.

PATIENT INVOLVEMENT

Patient DC has had author DR as her primary care physician since 2004, when she started taking buprenorphine for opioid use disorder; she continues to take it today. During this period, she received her nursing degree and has had two children. She was happy to share her experience of opioid use disorder but preferred to remain anonymous. She provided her perspective to the authors (summarized in separate box) and reviewed the manuscript. She had no suggestions for changes.

PATIENT COMMENTARY

I was a good kid and a good student and I graduated from high school in the top 10% of my class. I had a variety of jobs to support me while I was in college. I got a job in a bar that paid well but the coworkers were drinking, snorting cocaine, and taking opioid pills. This is how I started taking these drugs and became addicted. I first tried to get off drugs by detoxing by myself when I was 22. Then I tried outpatient detox twice, but that did not work. I then went to a three day inpatient detox but started using again after I left. Finally, after my older brother was murdered, I went to the emergency department and told them I was suicidal. I was admitted to a psychiatric unit and was started on methadone and went to a methadone program. I stayed on methadone for about a year and I was able to stay off other drugs.

I decided to try buprenorphine after I got a good job but I would have to take three buses to get to the methadone program and two buses from the program to my job. My counselor at the program told me of a clinic which was close to my house where I could be prescribed buprenorphine, because she saw that I was trying to get off the methadone, but she didn't feel I was ready to be without anything. Being on buprenorphine has changed my life completely. Without it, I would have probably relapsed and be dead. Having it as my safety net and with a great support system, I now have two children with my husband, I am a registered nurse, received my BSN, and bought my own home two years ago. It also has made me a better clinician because I've already been where the patients are, so I know exactly where they're coming from and I can relate to their situation.

Getting treatment in a primary care clinic is convenient and I can also get help with my other medical problems at the same time. This helps with my busy schedule. It also helps maintain my privacy. When I was going to a methadone program every day, other people would see me. This way, I am going to a primary care clinic once a month or every few months and no one knows why I am going there. Also, when I was going to a methadone program, I had to stand in line to be given medication and felt like I was just a number, but at the clinic, I feel I am treated like a person.

RESEARCH QUESTIONS

- What interventions can help to increase the provision of pharmacotherapy for opioid use disorder in primary care settings?
- How do we determine which psychosocial interventions are effective for which patients, and which patients need pharmacotherapy?
- What are the long term outcomes for patients treated with extended release pharmacotherapies in primary care settings (particularly extended release buprenorphine and naltrexone)?
- What are optimal ways to integrate patient centered approaches to care into treatment?

Christine Caufeld Noll did the initial literature search on behalf of authors.

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