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Opioid Addiction and Abuse in Primary Care Practice: A Comparison of Methadone and Buprenorphine as Treatment Options

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Abstract

Opioid abuse and addiction have increased in frequency in the United States over the past 20 years. In 2009, an estimated 5.3 million persons used opioid medications nonmedically within the past month, 200 000 used heroin, and approximately 9.6% of African Americans used an illicit drug. Racial and ethnic minorities experience disparities in availability and access to mental health care, including substance use disorders.

Primary care practitioners are often called upon to differentiate between appropriate, medically indicated opioid use in pain management vs inappropriate abuse or addiction. Racial and ethnic minority populations tend to favor primary care treatment settings over specialty mental health settings. Recent therapeutic advances allow patients requiring specialized treatment for opioid abuse and addiction to be managed in primary care settings. The Drug Addiction Treatment Act of 2000 enables qualified physicians with readily available short-term training to treat opioid-dependent patients with buprenorphine in an office-based setting, potentially making primary care physicians active partners in the diagnosis and treatment of opioid use disorders.

Methadone and buprenorphine are effective opioid replacement agents for maintenance and/or detoxification of opioid-addicted individuals. However, restrictive federal regulations and stigmatization of opioid addiction and treatment have limited the availability of methadone. The opioid partial agonist-antagonist buprenorphine/naloxone combination has proven an effective alternative. This article reviews the literature on differences between buprenorphine and methadone regarding availability, efficacy, safety, side-effects, and dosing, identifying resources for enhancing the effectiveness of medication-assisted recovery through coordination with behavioral/psychological counseling, embedded in the context of recovery-oriented systems of care.

Keywords

substance; abuse/use

The Surgeon General's Report *Mental Health: Culture, Race, and Ethnicity* highlighted the importance of addressing mental health and substance abuse disparities in racial and ethnic minority groups.¹ Persons from racial and ethnic minority groups often have less access to needed health care, are less likely to receive treatment, and the care that they receive is more likely to be of poorer quality. Although there is inconsistency in the data, in most cases, there are not significant differences in rates of mental disorders or substance abuse disorders among different racial and ethnic groups within the United States. Lillie-Blanton et al demonstrated that apparent racial differences in crack cocaine use disappeared when researchers controlled not only for individual income but also for neighborhood (contextual) poverty.² There are, however, some racial/ethnic differences in short-term trends (for example, the rising rate of injection drug use (IDU) of heroin among whites but not among African Americans.³

The overall impact of mental disorders and substance use (particularly opioid abuse and addiction) is far-reaching. The estimated societal costs of prescription opioid misuse totaled \$8.6 billion in 2001. Among commercially insured clients, annual direct health care costs in the years 1998–2002 approached \$16 000 per person for opioid abusers vs \$1800 for all others.⁴ Persons who use opioid drugs improperly miss over twice as many days of work monthly as nonusers.⁵

In a national epidemiologic study, Hatzembuehler found that compared to whites, blacks with co-occurring mood or anxiety and substance use disorders were significantly less likely to receive services for mood or anxiety disorders, equally likely to receive services for alcohol use disorders, and more likely to receive some types of services for drug use disorders.⁶ Once engaged in treatment, minority clients have rates of return visits similar to those of majority clients, so overcoming the barriers to engagement is essential.⁷ Among individuals with dual diagnoses (substance abuse and co-occurring mental health diagnoses), minority groups often access treatment in primary care settings rather than in specialty mental health clinics.⁸

Because primary care physicians are likely to encounter mental health and substance use disorders in their practice, it is important to delineate what can and cannot be appropriately managed in a primary care setting. Therefore, the authors undertook a review to help educate primary care providers on issues pertaining to treatment of opioid addiction and abuse. Studies included in this narrative literature review were identified by keyword searches of OVID, PubMed, and Google Scholar databases. Searched keywords included *methadone*, *buprenorphine*, *buprenorphine-naloxone*, *opioid*, and *opiate*. Manual searches of other relevant journals and texts (*Principles of Addiction Medicine, Third Edition*) and primary article reference lists were also conducted.

New evidence-based improved treatment modalities give primary care physicians the option of remaining engaged as a partner in drug treatment rather than simply referring for

treatment.⁹ Many patients choose the strategy of medication-assisted recovery,¹⁰ but Knudsen and Roman found that addiction treatment programs with higher proportions of minority patients were *less* likely to offer pharmacologic support for recovery.¹¹ The expanding array of pharmacologic interventions for addiction in the United States currently includes methadone and buprenorphine for opioid addiction, each agent having specific advantages and disadvantages.

Prevalence of Opioid Addiction

An estimated 5.3 million persons reported nonmedical use of pain relievers in the previous month in 2009, and there were an estimated 200 000 heroin users that year. An estimated 9.6% of African Americans¹² used some form of illicit drug in 2009. Opioid misuse prevalence doubled from 1977 to 1982, then increased more than 4-fold¹³ in the years 1987–1996. Recent Substance Abuse and Mental Health Services Administration (SAMHSA) surveillance data demonstrated a 13.6% lifetime prevalence of nonmedical prescription opioid use, with 5.9% of men and 4.2% of women reporting previous-year misuse.¹⁴

Prevalence of opioid misuse in primary care settings is difficult to estimate. Patients are characteristically secretive about misuse. In a study of 904 chronic pain patients receiving opioids in these settings, 80.5% reported at least 1 lifetime aberrant drug behavior. Most predictive of substance misuse were early refills (41.7%), increasing dose without physician consent (35.7%), and oversedation/intoxication from opioids¹⁵ (32.2%). The *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* criteria for current opioid dependence was met by 9.9% of patients with 4 or more aberrant drug behaviors¹⁵ (29.3%). Many patients using illicit opioids initially used legal prescriptions.¹⁶ State-specific data from the Centers for Disease Control and Prevention (CDC, 2008) reported that 20.8% of all Utah adults had received prescriptions for opioid pain medication within the previous year, and, of these, 3.2% had used more frequently or in higher doses than prescribed. Of those with leftover medication, 71% saved it for future use.¹⁷ A total of 1.8% of adults reported having used opioids that had been prescribed to someone else. Young adults were at increased risk of nonmedical opioid use, which significantly increases the risk of future substance use disorders.¹⁸

SAMHSA's Drug Abuse Warning Network data (2004–2008) showed a 111% increase in emergency department visits for nonmedical opioid use. Visits involving benzodiazepines, a common cause of fatal drug interactions with opioids, also increased.¹⁹ Opioid abuse and dependence often co-occurs with poly-drug abuse and mental illness comorbidities, especially affective disorders such as major depression and bipolar disorder. Anxiety disorders are also common in opioid misusing populations. Among the 5% of Americans who reported nonmedical opioid use, 30% were poly-drug users.²⁰ Recognition of co-occurring substance use and mental health disorders, known as *dual diagnosis*, is critical in primary care settings. For this reason, the Alcohol Use Disorders Identification Test, the CAGE Questions Adapted to Include Drugs (CAGE-AID) and the Patient Health Questionnaire-9 (PHQ-9) are potentially valuable screening tools. Many times, management of identified comorbidities can be accomplished by means of referral to specialty mental health treatment programs.

Screening and Identification of Opioid-Misusing Patients

As many as 1 in 3 opioid-maintained pain patients may crossover into inappropriate use. These patients frequently have challenging personality traits and may be perceived as “manipulative, drug-seeking, and noncompliant.”²¹ However, tolerance to opioid analgesia normally develops over time, so the need for increasing opioid dosage may not necessarily indicate drug misuse.

Validated screening tools are available to assess substance use severity. One approach to identifying patients with opioid abuse/addiction is to implement screening, brief intervention, and referral to treatment (SBIRT).²² SBIRT is an integrated approach aimed at delivering early intervention and treatment services. Individuals identified as moderate-risk may undergo brief intervention via the primary care provider, with more severe cases referable to a substance abuse treatment specialist.

Assessment of addiction severity is essential. Measures of addiction severity may help the primary care physician to assess potential risks of diversion as well as to decide whether to attempt in-house treatment or to refer to an addiction specialist. The widely used Addiction Severity Index (ASI) is adapted to both alcohol (ASI-alc) and drug addiction (ASI-drug). Other available diagnostic and screening instruments include the Clinical Opiate Withdrawal Scale (COWS), the Subjective Opiate Withdrawal Scale (SOWS), the Drug Abuse Screening Test (DAST), the Clinical Institute Narcotic Assessment Scale for Withdrawal Symptoms (CINA) the CAGE-AID, and the Narcotic Withdrawal Scale.

Differentiating Opioid Misuse From Appropriate Use for Pain Control

Often, primary care practitioners must differentiate between opioid tolerance induced by appropriate pain management and abuse or addiction.²³ Available tools for close monitoring of at-risk chronic pain patients include self-report instruments (Prescription Drug Use Questionnaire), physician assessment tools (Addiction Behavior Checklist), and urine drug screenings.^{24,25} Specific tools related to monitoring opioid use in pain patients include the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R), the Opioid Risk Tool, and the Pain Assessment and Documentation Tool.²⁶ Potential red flags for misuse of prescription opioids include a medical history suggestive of “doctor shopping,” running out of medications repeatedly, false claims of lost prescriptions, suspected theft of prescriptions/prescription pads, or possession of numerous opioid medication bottles. Family members or the practitioner may notice unexplained changes in personality, marked mood swings, and unusually pronounced drug side effects such as atypical drowsiness, marked constipation, or confusion. Suspicious behaviors regarding medication intake include taking more medication than prescribed or more often than prescribed and signs of taking medications in an unusual way, such as unexplained needle marks or nasal problems, possibly due to crushing and snorting pills. Changes in social behaviors may include changes in networks of friends, declining grades, frequent disciplinary actions or abandonment of favored extracurricular activities in school, excessive absenteeism, or failing job performance.^{27,28}

Urine drug screening has remained the most common and convenient method of identifying the covert use of illicit drugs. However, urine drug screening methodology has several inherent limitations. The temporal window of detection is limited to only 2 to 3 days for most drugs. Adulteration, specimen substitution, and other forms of tampering are possible and may be difficult to control. Owing to wide natural variations in urine concentration, detection of a drug in the urine may have little or no correlation with dose or time of administration.²⁹

Key Differences Between Methadone and Buprenorphine Treatment

Opioid addiction treatment with pharmacologically active opioids remains controversial.³⁰ The efficacy of methadone in reducing or eliminating heroin use has long been established, but methadone remains available principally in pain clinics and specialized dosing centers that may be geographically distant from users, especially users not residing in large cities.³¹ A review of state law and regulatory policies concluded that policy and prescribing law “has not kept pace with advancements in medical and scientific knowledge about the interface between pain management and addictive disease.”³²

Widespread availability of buprenorphine offers a distinct advantage over methadone.³³ The Drug Addiction Treatment Act of 2000 permits physicians to treat up to 30 patients with buprenorphine in office-based settings. A Drug Enforcement Administration–licensed physician can obtain credentials to prescribe buprenorphine by taking a readily available 8-hour training program online or in class.³⁴ Also, buprenorphine may be prescribed in the setting of a methadone maintenance clinic, in which case, the program may treat administration as similar to methadone with respect to observed ingestion, random urine drug screens, and earned take-home medication. Initially, an office-based practitioner may be allowed to prescribe buprenorphine preparations to a maximum of 30 patients. However, after 1 year of practice, permission may be obtained to increase the number of patients to 100 via physician request to SAMHSA.³⁵

Much of the general public is unfamiliar with buprenorphine and has little or no opinion about it, so the name carries less stigma than methadone. Qualitative interviews with 64 methadone maintenance clients revealed stigmatization experiences. Researchers concluded that reducing stigmatizing experiences may improve treatment outcomes and decrease barriers to treatment.³⁶

Public and media concern about methadone diversion and potential overdose hazards fuel political pressure to uphold strict and complex regulations on methadone service delivery.³⁷ Methadone clients typically must show treatment compliance for 2 years to be eligible to take home a month’s supply of medication. Buprenorphine has less-burdensome regulation and oversight requirements, allowing for home treatment sooner. However, buprenorphine is fairly expensive. A month’s supply of a typical sublingual daily dose of 8 to 24 mg may cost \$200 to \$450 per month.³⁸

High-dose buprenorphine has been shown to be more effective than low-dose methadone in client retention and illicit drug-free urine screen rates.³⁹ However, buprenorphine may not relieve subjective symptoms for patients who have used large quantities of opioids for a

considerable period of time. Even at high doses, buprenorphine only partially activates the opioid mu receptor to approximately 40% of full output.⁴⁰ In severely addicted patients, methadone, which activates the receptor fully, may be more efficacious therapeutically.⁴¹ High-dose-methadone-treated subjects remain in treatment longer, exhibiting longer periods of abstinence and more drug-free urine screenings than buprenorphine patients.⁴²

Buprenorphine is largely self-administered, causing concern about inadequate frequency of monitoring and urine drug screenings.⁴³ Some clients may purposely decide to use buprenorphine intermittently. In methadone clinics, patients receive random urine drug screenings. Those entrusted with 1 to 4 weeks of medication are subject to being called back randomly for urine drug screenings and milligram counts on remaining medication. Also, buprenorphine appears less effective than methadone in reducing or eliminating co-occurring opioid and cocaine dependence.⁴⁴

A meta-analysis of 37 studies involving a total of 3029 patients found that high doses of outpatient methadone had greater efficacy than lower doses in sustaining heroin abstinence, that methadone was preferable to buprenorphine for this purpose, and that outpatient methadone treatment can be efficacious in treating dual opioid and cocaine dependence, especially when combined with adjunctive agents such as indirect dopaminergic drugs and behavioral contingency management aimed at cocaine abstinence.⁴⁵

Buprenorphine's partial mu agonist activity may induce a milder withdrawal syndrome than most opioids; thus, discontinuing buprenorphine may be easier.⁴⁶ Buprenorphine is also a κ -receptor antagonist and therefore less apt to generate dysphoria. However, a misconception exists that people who taper off buprenorphine can easily remain drug-free thereafter. Like methadone, many patients who terminate treatment may not be able to sustain abstinence. Studies on opioid-related mortality demonstrate that risk of death is usually lowest during treatment but increases substantially in the first year after discontinuing either methadone or buprenorphine, principally from relapse consequences.⁴⁷ Key differences in efficacy are tabulated in Box 1.

Side Effects, Safety, and Tolerability

The side effect profile of buprenorphine appears milder overall than methadone. Methadone frequently causes chronic sweats, constipation, and sexual dysfunction. A study comparing sexual dysfunction in male patients dependent on heroin with those on methadone or buprenorphine found that fewer patients on buprenorphine reported loss of sexual fantasy or desire, loss of erection with movement, premature ejaculation, and loss of angulation of the penis.⁴⁸

Methadone has been used widely for more than 30 years; therefore, much is known about long-term effects. Buprenorphine was approved for opioid treatment in 2002, so the long-term effects of maintenance are less certain.

Buprenorphine exhibits poor gastrointestinal absorption (buprenorphine is administered sublingually in addiction treatment). Usually, buprenorphine is used as a combination preparation with naloxone (naloxone exhibits comparatively poor sublingual absorption) in

order to prevent illicit injection. Thus, buprenorphine poses much less overdose hazard if ingested intentionally or accidentally by nontolerant individuals.

Buprenorphine exhibits ceiling effects on respiratory depression due to its intrinsic agonist/antagonist effects.⁴⁹ This exceptional pharmacology offers an enhanced safety profile compared with methadone. However, buprenorphine-induced respiratory depression may be extremely difficult to reverse when it does occur. Fatal respiratory depression has been reported among addicts misusing buprenorphine intravenously, often with concomitant sedative drugs. In one study, 0.8 mg of intravenous naloxone was ineffective in reversing buprenorphine-induced respiratory depression.⁵⁰ Increasing naloxone to 2 to 4 mg given over 30 minutes was required to fully reverse buprenorphine's effect. A dose window effect was observed, as increasing the naloxone to 5 mg or greater led to a decline in reversal activity. Naloxone bolus doses of 2 to 3 mg, followed by continuous infusion of 4 mg/hr, led to full reversal within 40 to 60 minutes of both 0.2 and 0.4 mg intravenous buprenorphine-induced respiratory depression. Respiratory depression from buprenorphine may outlast the reversal effects of a naloxone bolus or short infusion, so sustained infusion may be required.

Chronic liver disease (especially hepatitis C) is extremely common in the United States among individuals who have shared injection equipment. Methadone maintenance has proven safe for patients with stable chronic liver disease, including advanced cirrhosis, often with little or no alteration in dose. However, sublingual buprenorphine is associated with elevated liver enzymes, more so with intravenous administration.⁵¹ Liver function should be monitored during buprenorphine treatment and clients should be warned against intravenous use.⁵² Fortunately, neither methadone nor buprenorphine appears to affect the safety and efficacy of interferon and ribavirin in the treatment of hepatitis C infection. Conversely, there are significant interactions with certain human immunodeficiency virus (HIV) antiretroviral treatments as well as the antibiotic rifampin.⁵³

The induction period, during which the drug is introduced at a low dosage and slowly titrated to the individual patient's therapeutic level, is considered the most dangerous time in treatment for methadone clients. The Pharmaceutical Drugs of Abuse System database records start and end dates of all cases of methadone and buprenorphine treatment in New South Wales, while the National Death Index documents all reported deaths.⁵⁴ Comparison showed that buprenorphine maintenance was not associated with increased risk of death.

Measurable diversion and misuse of buprenorphine have been observed multinationally in cases where buprenorphine has been prescribed for chronic pain, but numbers appear relatively small compared with conventional opioids. In such cases, pills typically have been crushed and injected, and some "doctor shopping" has been observed.⁵⁵

In Europe, buprenorphine-related deaths have been reported, mostly in association with benzodiazepine use.⁵⁶ However, buprenorphine may be somewhat less toxic than methadone in combination with benzodiazepines. Opiate/benzodiazepine-codependent patients reported less-severe withdrawal symptoms during buprenorphine treatment and were more likely to complete detoxification protocols.⁵⁷ In a direct comparison of 3349 patients on buprenorphine and 2643 patients on methadone, retention was significantly longer on

methadone (271 days) than buprenorphine (40 days). During induction, the risk of death was significantly lower for buprenorphine⁴⁰ (relative risk = 0.114). Comparative side effects are tabulated in Box 2.

Use in Pregnancy

The naloxone used in combination buprenorphine/naloxone preparations is classified in Food and Drug Administration pregnancy category C, and women may be exposed before pregnancy is recognized. The buprenorphine-only preparation is the recommended maintenance agent in pregnancy. However, buprenorphine may carry less risk than methadone for inducing neonatal abstinence syndrome in the offspring of treated women. Forty-seven prospectively followed pregnancies in 39 buprenorphine-treated women were compared with 35 retrospectively analyzed methadone-exposed pregnancies.⁵⁸ The buprenorphine-exposed pregnancies resulted in 47 uneventful live births with normal birth weights, including 2 sets of twins, 1 unexplained stillbirth and 1 miscarriage. Typically mild neonatal abstinence syndrome occurred in 40.4% of infants, with only 14.9% needing treatment. Of the 35 methadone-exposed infants born at the same hospital, 77.8% exhibited neonatal abstinence syndrome, with 52.8% needing treatment. On average, buprenorphine pregnancies exhibited longer gestation, higher birth weights, lower frequency and severity of neonatal abstinence syndrome, and shorter hospital stays. A recent double-blind randomized controlled trial of buprenorphine vs methadone in 175 pregnant women at 8 international sites confirmed that buprenorphine resulted in a lower need for morphine and shorter hospital stays related to the neonatal abstinence syndrome.⁵⁹

Abuse Potential and Drug Diversion

Buprenorphine appears less subject to diversion than methadone owing to intrinsic opioid-blocking effects and widespread use in combination with naloxone. Buprenorphine alone has been abused intravenously, and even combination buprenorphine/naloxone preparations can be misused.⁶⁰ However, in a survey of untreated intravenous opioid drug users conducted at a Helsinki needle exchange program, 68% had tried combination buprenorphine/naloxone intravenously, but 80% reported having had a “bad” experience.⁶¹ The street price of buprenorphine/naloxone was less than half that of buprenorphine alone.

Dosing and Administration—Acute Induction/Withdrawal

Buprenorphine has a shorter plasma half-life than methadone but exhibits very slow pharmacokinetic dissociation from the mu receptor.⁶² This high affinity can produce protracted therapeutic action, even allowing for dosing every 2 or 3 days in certain patients. Methadone patients typically need daily dosing, with some rapidly metabolizing patients requiring multiple daily doses.

In office-based buprenorphine treatment, logistics may pose problems for some practitioners. Buprenorphine induction requires titration with repeated small doses given over 1 to 3 entire mornings until a comfort level is reached. Practitioners may have to dedicate an entire room to the patient or leave them symptomatic in the waiting room, which

may be disturbing to other patients. In methadone clinics, a single daily dose is given, with titration occurring over several weeks.

Buprenorphine induction must be performed while the patient is withdrawing from other opioids. If induction is attempted when the person is not in sufficient withdrawal, mu-antagonist effects will predominate and intensify rather than relieve withdrawal symptoms. The patient may move precariously between lacking immediate relief and risking buprenorphine-precipitated withdrawal. In a series of 103 outpatient buprenorphine inductions, 5 cases of mild to moderate buprenorphine-prompted withdrawal and 8 cases of prolonged unrelieved withdrawal symptoms were reported.⁶³

Home-based induction with buprenorphine is another option. Current guidelines recommend direct observation of initial dosing of buprenorphine with a subsequent series of clinic visits for induction. However, there is some limited evidence to support the efficacy of home-based induction, with results of participants who underwent at-home inductions having similar outcomes to standard office-based inductions.^{63,64}

There is limited clinical experience in treating acute pain in buprenorphine patients. Since buprenorphine is a partial antagonist with very high mu-receptor affinity, pain treatment is seriously complicated when other opioid analgesics are administered concurrently or sequentially.⁶⁵ Other opioids are often limited in their ability to displace buprenorphine from the mu receptor or to counter its antagonistic effects. Difficulties in clinical management of acute pain as a result of trauma or illness may occur among buprenorphine-maintained patients. A number of approaches have been suggested, such as titrating full opioid mu agonists while carefully monitoring level of consciousness, but this remains a very challenging situation for which clear guidelines are lacking.

Treat or Refer?

In a qualitative study examining primary care physicians' attitudes towards integrating buprenorphine treatment into their individual practices, reported incentives included greater continuity of patient care and buprenorphine as a positive alternative to methadone.⁶⁶ Disincentives included competing activities, lack of interest, lack of expertise in addiction, lack of remuneration, inadequate ancillary support, time limitations, and a perceived low prevalence of opioid dependence in their practices. Physicians felt that patients would have concerns about confidentiality and cost and might lack motivation for treatment. Greater incentives and/or technical support may be needed to facilitate extension of buprenorphine maintenance therapy into more primary care- and office-based practices.

Recovery-Oriented Systems of Care

A purely pharmacologic approach to medication-assisted recovery is rarely, if ever, sufficient. The integration of addiction treatment into patient-centered primary care appears to improve treatment outcomes.⁶⁷ Buprenorphine/naloxone treatment alone is less effective than medical management plus professional behavioral drug counseling.⁶⁸ Broader psychosocial strategies enhance recovery even more.⁶⁹ Recovery-oriented systems of care are individual-centered, self-directed approaches to recovery that build on the sum total of

recovery support resources in a community. These include physicians, counselors, family, faith-based organizations, support groups, intimate social networks, community-based institutions, peer support, schools, and workplaces working in collaboration to provide flexible, culturally sensitive and adaptable services providing continuity of care for recovering people in achieving and maintaining lifelong sobriety.⁷⁰ The American Association of Community Psychiatrists has developed Guidelines for Recovery Oriented Services in order to operationalize this model.⁷¹ The Center for Substance Abuse Treatment of SAMHSA also emphasizes recovery-oriented systems of care. SAMHSA-funded Addiction Technology Transfer Centers are a rich source of tools and resources for the primary care clinician related to recovery-oriented systems of care, SBIRT, buprenorphine, and other treatment modalities (Box 3).

Conclusion

Buprenorphine and methadone each have specific advantages and disadvantages. Neither is likely to completely replace or render the other obsolete. Properly and judiciously used, either agent can help suitably selected patients avoid illicit opioid use while improving mental health and quality of life.⁷² The decision as to which medication is indicated must be guided by the unique addiction history, personal characteristics, life situation, and therapeutic responsiveness of the individual patient. Primary care providers must be equipped to manage both mental health and substance use disorders within their practice settings, as the majority of the population with substance use disorders will seek behavioral health and substance abuse treatment from their primary care providers, rather than at specialty mental health and substance abuse treatment facilities.

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Box 1. Effectiveness of Buprenorphine vs Methadone

Buprenorphine	Methadone
Partial mu agonist	Full mu agonist
Limited withdrawal relief in heavy and/or long-term opiate users.	Titratable withdrawal relief (even in heavy and/or long-term opiate users)
Widely available but high-cost	Limited availability, lower cost
Less retention in treatment	Greater retention in treatment
Lower diversion risk, especially in combination preparation containing naloxone	Higher diversion risk
Patient self-administration typical	More frequent supervised administration
Less effective in co-occurring opiate and cocaine dependence	More effective in co-occurring opiate and cocaine dependence
Less monitoring required (e.g. urine drug screens)	High monitoring, frequent urine drug screens

Box 2. Side Effects: Comparison of Buprenorphine and Methadone

Buprenorphine	Methadone
Less risk of sexual dysfunction	Greater risk of sexual dysfunction
Less risk of respiratory depression but more difficult to reverse if present	Greater risk of respiratory depression, more readily reversible if present
Deaths during induction phase very rare	Higher risk of death during induction phase
May raise liver function tests	Proven safe in chronic liver disease
If more analgesia required, may block other opiate analgesics in pain treatment	Highly effective in pain treatment
Partial antagonist to other opiates	Pure opiate agonist
Lower risk of neonatal abstinence syndrome	Higher risk of neonatal abstinence syndrome
Less κ effect, lower risk of dysphoria	More κ effect, higher risk of dysphoria
Poor oral absorption, less overdose risk in diversion	Well absorbed orally, higher overdose risk in diversion
Lower risk of dependence	Higher risk of dependence
Lower risk of death with benzodiazepines	Higher risk of drug interaction fatalities with benzodiazepines

Box 3. Resources for the Primary Care Physician

Web-based buprenorphine training information

- American Academy of Addiction Psychiatry, www2.aaap.org/buprenorphine
- American Society of Addiction Medicine, www.asam.org/BuprenorphineCME.html
- Substance Abuse and Mental Health Services Administration buprenorphine training, <http://buprenorphine.samhsa.gov/pls/bwns/training>
- Other buprenorphine training, www.buppractice.com/

Managing opioid addiction with buprenorphine (summary for patients in *Am Fam Physician.*),¹
www.ncbi.nlm.nih.gov/pubmed/16719249

Buprenorphine Treatment Facility Locator, http://buprenorphine.samhsa.gov/bwns_locator/

Drug and Alcohol Abuse Treatment Facility Locator, <http://dasis3.samhsa.gov/>

TIP 24: A Guide to Substance Abuse Services for Primary Care Clinicians Treatment Improvement Protocol (TIP) Series 24, www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=hssamhsatip&part=A45293

Addiction Technology Transfer Center Network, www.attcnetwork.org/index.asp

Recovery in the Community: An Emerging Framework—A Recovery-Oriented Systems of Care Approach. (NASADAD) (45pp, PDF, 431KB), <http://pfr.samhsa.gov/rosc.html>

An Emerging Framework—A Recovery-Oriented Systems of Care Approach (NAADAC) (46 pp, PDF, 438 kb), http://partnersforrecovery.samhsa.gov/docs/NADDAC_presentation_0608.pdf

The American Association of Community Psychiatrists has developed Guidelines for Recovery Oriented Services in order to operationalize ROSC, [www.communitypsychiatry.org/publications/clinical_and_administrative_tools_guidelines/ROSGuidelines.pdf#search="recovery oriented services"](http://www.communitypsychiatry.org/publications/clinical_and_administrative_tools_guidelines/ROSGuidelines.pdf#search=)

The Center for Substance Abuse Treatment of the Substance Abuse and Mental Health Services Administration, <http://csat.samhsa.gov/treatment.aspx>

SAMHSA-funded addiction technology transfer centers are a rich source of tools and resources for the primary care clinician related to recovery-oriented systems of care; screening, brief intervention, and referral to treatment; buprenorphine; and other treatment modalities, www.attcnetwork.org/index.asp

A mentorship program for the buprenorphine prescriber and additional resources, www.pcssb.org/mentors-and-mentees/