

Resource Document on the Treatment of Opioid Use Disorder in the General Hospital

Approved by the Joint Reference Committee, October 2022

“The findings, opinions, and conclusions of this report do not necessarily represent the views of the officers, trustees, or all members of the American Psychiatric Association. Views expressed are those of the authors.” – *APA Operations Manual*

This Resource Document explores the pharmacology of opioid use disorder (OUD) treatment, education around OUD and its management, specialty-specific concerns, barriers to care, and an approach to reduction of stigma. While the APA recognizes that the topic of OUD treatment is broad and deserves nuanced attention, the scope of this Resource Document is limited to treatment of OUD in the general hospital.

Prepared by the Council on Consultation-Liaison Psychiatry and the Council on Addiction Psychiatry

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INTRODUCTION

The morbidity, mortality, and cost of opioid use disorder (OUD) have dramatically increased over the past two decades, necessitating a call to action for all health care systems and health care providers, regardless of specialty, to reassess the approach to OUD treatment. According to the Centers for Disease Control and Prevention (CDC), from 1999 to 2018, opioids were involved in 446,032 deaths in the U.S., with 67,367 deaths in 2018 alone (1). In 2019, among people 12 years and older in the U.S., 0.6% (1.6 million people) had an opioid use disorder. Of those, only 18.1% (294,000 people) received medication for opioid use disorder (MOUD). In the same year, among adults 18 years and older with any mental illness and serious mental illness, 8.8% and 13.8% used opioids (heroin use or prescription opioid misuse), respectively (2).

Patients with OUD may first engage in treatment through a variety of entry points into the health care system, including the emergency department, general hospital, inpatient psychiatry unit, outpatient clinic, harm reduction services (e.g., syringe exchange services, supervised injection sites), or the criminal justice system. The inpatient general hospital is an especially important point of focus given the significant medical comorbidity of OUD and the financial impact on the health care system. In 2018, among U.S. adults 18 years and older, there were 748,900 opioid-related inpatient hospital stays (without concurrent stimulant use) accounting for 296 hospital stays per 100,000 population, representing an increase of 30.8% from 2012 (3). It is essential to actively engage patients with OUD in the general hospital setting where there may be more time and resources to develop and initiate a treatment plan in collaboration with the specialty services treating the medical comorbidities of the OUD. The role of the psychiatrist, as an expert in the treatment of substance use disorders (SUD), comorbid psychiatric illness, and harm reduction strategies, can be of great benefit to the hospital team. Unfortunately, and for many reasons, the psychiatrist is often not a member of the treatment team. The absence of psychiatry may be due to prevailing hospital culture, lack of local psychiatry consultation-liaison services, the presence of other specialty services that have “owned” the role, psychiatrists’ lack of comfort and education treating the OUD population, and lack of knowledge about the scope of psychiatry by consulting members of the treatment team.

To address these gaps, the American Psychiatric Association (APA) Council on Consultation-Liaison Psychiatry, in collaboration with the APA Council on Addiction Psychiatry, convened an expert workgroup with representation from the Academy of Consultation Liaison Psychiatry (ACLP), the American Academy of Addiction Psychiatry (AAAP), and the Association of Medicine and Psychiatry (AMP) to prepare a unified resource about treatment of OUD for psychiatrists practicing in the general hospital setting. To best inform the process, the workgroup convened a roundtable discussion in December 2020 that officially identified representatives from specialty organizations who have high stakes in the best-practice, in-hospital treatment of patients with OUD, including the American Society of Addiction Medicine (ASAM), the Infectious Diseases Society of America, the American College of Obstetrics and Gynecology (ACOG), the American College of Surgeons (ACS), the American College of Emergency Physicians, and the American Hospital Association. Representatives from the stakeholder organizations were asked to discuss specialty-specific challenges of treating patients with OUD, common clinical scenarios where patients with OUD are encountered, formal guidelines or accepted best-practice treatment paradigms, harm reduction strategies, and the recommended role of the in-hospital psychiatrist. These critical insights were used to develop the framework of this Resource Document.

In addition to many important specialty-specific themes that will be discussed below, several threads emerged from the roundtable discussion across all specialties. First, psychiatry is underrecognized as the “owner” of substance use disorder treatment; in fact, most specialties identify Addiction Medicine

and/or Pain Medicine as the primary specialists for SUD treatment. The ACS noted that psychiatry is rarely considered to assist with these patients because of sheer lack of knowledge that psychiatrists treat addiction. This insight suggests that the specialty of psychiatry may have an inaccurate and one-sided impression of “ownership” of SUD treatment in the general hospital that requires examination. Second, the stigma associated with SUDs continues to be a barrier to care across all parts of health care and may impact systems-level decisions about policy and allocation of resources. Within psychiatry, close attention is needed to our roles as collective contributors to this stigma, with consideration of *why* psychiatry has not proudly owned this field or required the education necessary for psychiatrists to be current in treating and educating others about OUD. Third, there is a widespread education gap across specialties that begins in medical school and is reinforced in post-graduate training through the absence of well-defined competencies (4) for treating the patient with a SUD. Finally, there are abundant opportunities for high-impact collaboration across specialties to educate and advocate for this high-risk population.

Recognizing that the topic of OUD treatment is broad and deserves nuanced attention, the scope of this Resource Document is limited to treatment of OUD in the general hospital. The document will explore the pharmacology of opioid use disorder treatment, education around OUD and its management, specialty-specific concerns, barriers to care, and an approach to reduction of stigma. The roles of comorbid substance use, comorbid mental illness, and the approach to treatment in children are not discussed within this resource.

This Resource Document is not intended to be a clinical practice guideline (CPG); rather, it is an educational tool for clinicians to use when treating patients with OUD in the general hospital setting. To date, 28 CPGs have been developed by various organizations and societies, both nationally and internationally. However, these are of variable scope, methodological rigor, applicability, and detail (5). The five “recommended” CPGs found to have highest overall quality using Appraisal of Guidelines for Research and Evaluation (AGREE-II) criteria (6) are notably those from Canada and the World Health Organization (WHO) (7-11), with guidelines from U.S. organizations including American Society of Addiction Medicine (ASAM) (12), Substance Abuse and Mental Health Services Administration (SAMHSA) (13), and American College of Obstetricians and Gynecologists (ACOG) (14) found to be “recommended with modifications” (5). Where applicable, we refer specifically to relevant CPGs.

OVERVIEW OF PHARMACOLOGIC TREATMENT

For psychiatrists to take ownership of the treatment of medically hospitalized patients with OUD, it is essential to appreciate both the scope and intricacies of the pharmacologic options available for medical management. This section will review buprenorphine, methadone, and naltrexone (see Table 1), as well as in-hospital treatment protocols.

1. Buprenorphine

Buprenorphine is a semisynthetic opioid approved for opioid use disorder (OUD) with a unique set of pharmacologic and pharmacokinetic properties. It is a complex lipophilic molecule derived from the opium alkaloid *Papaver somniferum* (15). It was originally developed in the 1970s as an analgesic (16) and subsequently investigated for addiction treatment given its unique pharmacology (high opioid receptor affinity, lower pharmacologic efficacy, and slow opioid receptor dissociation). It is a Schedule III medication approved in the United States in 2002 for treatment of OUD. Unlike traditional opioids, which are agonists at all opioid receptors, buprenorphine is often described as a mixed agonist-antagonist given its binding profile across opioid receptors to which it displays high binding affinity (Figure 1). At the μ -opioid receptor (MOR) it is a partial agonist; at the kappa-opioid receptor (KOR) it is

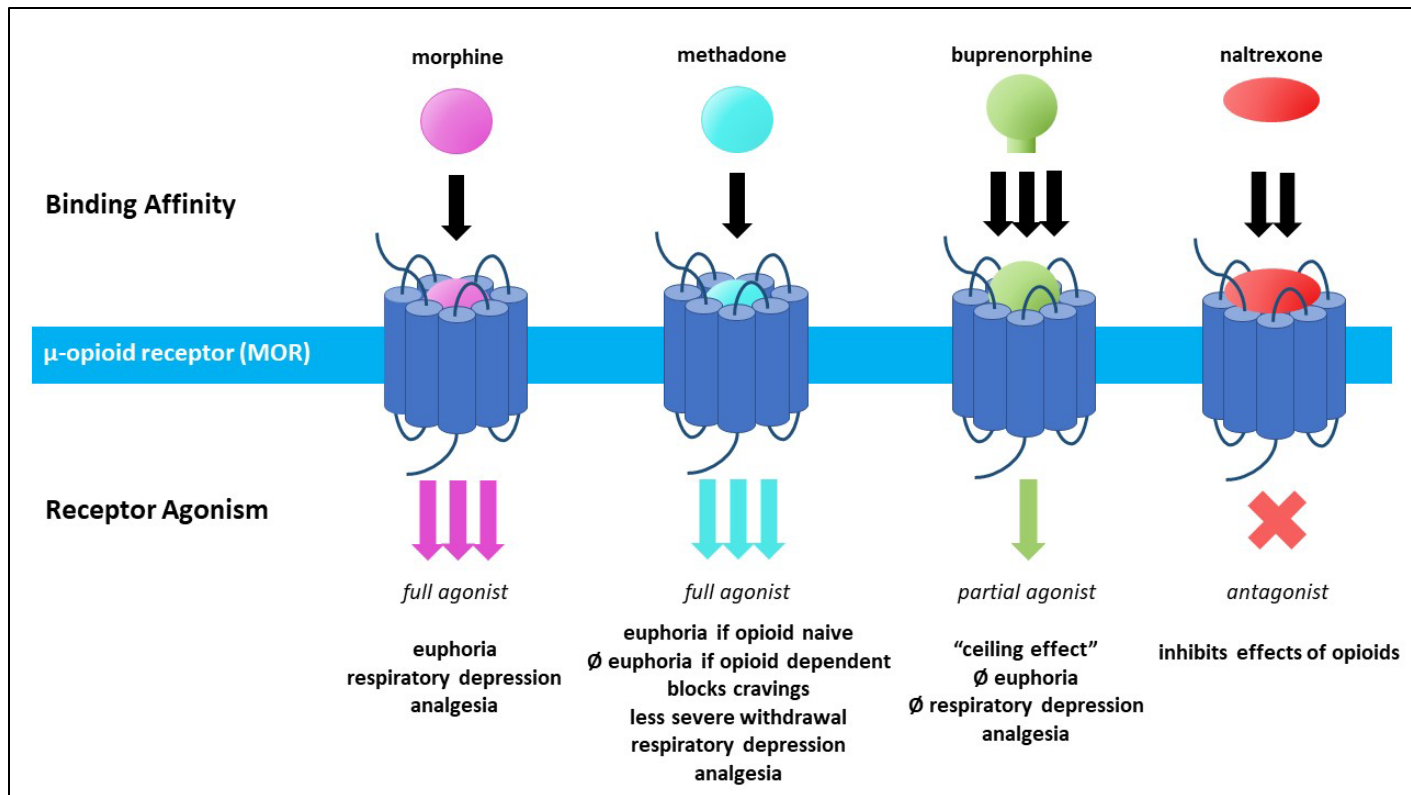
an inverse agonist; and at the delta-opioid receptor (DOR) it is an antagonist. Notably, it is also an agonist with low binding affinity for the opioid receptor-like 1 receptor (17). Because it is a partial μ -agonist, it does not fully activate the receptor, which results in decreased typical effects from full-agonist therapy and an improved safety profile. Clinically, this results in decreased euphoria elicited by opioids, which in turn decreases the abuse liability. It also exhibits a “ceiling effect” to the pharmacological effect of respiratory depression (regardless of the amount ingested), which subsequently reduces the risk of respiratory compromise in overdose (18). Buprenorphine’s affinity for the MOR is approximately 1.7 times that of hydromorphone, 5.4 times that of morphine, 6.7 times that of fentanyl, and 120 times that of oxycodone (19). This high MOR affinity makes it difficult to displace buprenorphine from the opioid receptor and allows buprenorphine to displace other full opioid-agonists, which can lead to precipitated withdrawal (20).

Buprenorphine is a high-potency medication, meaning a small amount can produce a significant effect. Potency depends on efficacy and affinity. This concept is important in understanding why buprenorphine should not be converted to morphine milligram equivalents (MME), either for purposes of rotating opioid analgesic or for assessing risk of overdose. Buprenorphine has slow dissociation kinetics that contribute to its long duration of action and allow for once-daily dosing. Bioavailability depends on specific product but is approximately 30% for sublingual administration. The half-life of buprenorphine varies depending on route of administration. The half-life after transmucosal administration ranges from 24 to 42 hours, while the half-life after IV administration is approximately 3 hours (20).

2. Methadone

Methadone is a synthetic opioid approved for OUD with a complex pharmacological profile: it is a full agonist at the MOR, is an N-methyl-D-aspartate receptor antagonist and has serotonin-norepinephrine reuptake inhibition activity. It was originally approved by the Food and Drug Administration (FDA) in 1947 for its analgesic and antitussive properties, but was not approved until 1972 in the United States for the treatment of OUD, despite a landmark study in 1965 that demonstrated this effect. This approval has remained strictly regulated, with methadone available only in federally licensed and accredited opioid treatment programs.

Figure 1. Activity of Medications for OUD at the μ -Opioid Receptor



Unlike buprenorphine, methadone is a full agonist at the MOR, and as such, it creates no risk of precipitating withdrawal with administration. Methadone does not have the “ceiling effect” seen with buprenorphine, making the risk of respiratory depression an important consideration. Methadone has wide inter- and intra-patient variability with respect to its pharmacokinetic properties. It is highly lipophilic, lending itself to once-daily administration, and has a long and variable terminal half-life (5-130 hours), while its analgesic effects last only 4-8 hours (21). When titrating methadone, it is important to monitor closely, as the respiratory depressant effects peak later and last longer than its analgesic effects. Fatal overdose can occur if it is titrated too quickly. A person does not have to be in withdrawal prior to initiation, but in most inpatient settings, dosing begins when withdrawal symptoms are present to confirm physical dependence.

3. Naltrexone

Naltrexone is a synthetic derivative of oxymorphone but acts as a competitive MOR antagonist. The oral version of naltrexone was approved in 1984 for OUD, while the injectable version was approved for alcohol use disorder in 2006 and for OUD in 2010. Oral naltrexone use is limited by its high rates of non-adherence, while the injectable version has been shown to be non-inferior to buprenorphine after medically supervised withdrawal. Naltrexone has few intrinsic properties other than opioid receptor antagonism, and its pharmacokinetic properties are simple. Its half-life depends on formulation (oral: 4 hours; injectable: 5-10 days) due to extensive first-pass metabolism after oral administration to active metabolite, 6-beta-nalrexol. It is widely distributed and relies on renal elimination. Naltrexone can be hepatotoxic, with elevations of transaminases occurring in 14-20% of patients, although progression to liver failure is rare. The Department of Veterans Affairs/Department of Defense Guideline (22) for the Treatment of Substance Use Disorders recommends obtaining baseline transaminases prior to initiation, at 6 and 12 months, and avoiding use in patients with acute hepatitis or liver failure. A baseline bilirubin and beta-hCG (for females) are also recommended.

4. Naloxone

Naloxone is a competitive opioid antagonist that displaces opioids and is used to treat opioid overdose. It has been FDA approved since 1971 in intravenous and intramuscular formulations. In the late 1990s, several states piloted take-home naloxone kits to prevent opioid overdoses, and in 2015 the nasal spray gained FDA approval. The different formulations vary in onset of action, but all have a short half-life such that repeated doses may be necessary depending on the opioid consumed. Naloxone is largely considered a safe medication with no recommended dosage adjustments. Its wide distribution has been associated with significant decreases in opioid overdose deaths (23).

Often naloxone is co-administered with buprenorphine as a single agent, buprenorphine/naloxone. It is often claimed that the naloxone component of the combined agent will precipitate withdrawal if injected, serving as a deterrent against misuse. However, buprenorphine has a higher binding affinity and longer elimination half-life than naloxone. It is more plausible that any withdrawal would be caused by full agonist displacement by buprenorphine rather than naloxone.

Table 1. Summary of Medications for Treatment of Opioid Use Disorder

Receptor Binding	Benefits	Disadvantages	Drug Interactions
Buprenorphine			
High affinity at μ -, κ -, and δ -opioid receptors	“Ceiling effect” results in decreased euphoria, abuse liability, and risk of respiratory compromise in overdose	Displacement of other full agonists may precipitate withdrawal	Metabolized by CYP3A4
μ -opioid receptor (MOR): partial agonist		Requires waiver to prescribe	Withdrawal may occur if co-administered with a CYP3A4 inducer (e.g., rifampin, phenytoin, phenobarbital, carbamazepine, St. John’s wort)
κ -opioid receptor (KOR): inverse agonist	Can be obtained at normal pharmacies in convenient quantities		Toxicity may occur if co-administered with a CYP3A4 inhibitor (e.g., azole antifungals, macrolide antibiotics, some selective serotonin reuptake inhibitors, atazanavir)
δ -opioid receptor (DOR): antagonist	Limited data suggests safe in pregnancy		Toxicity or withdrawal with discontinuation of a CYP3A4 inducer or inhibitor respectively
Opioid receptor-like 1 receptor: agonist (low affinity)	Acute and chronic analgesic effects like full agonist opioids		Co-administration with serotonergic drugs may result in serotonin syndrome
			Caution when used with other central nervous system depressants (e.g., benzodiazepines)
Methadone			
MOR: full agonist	No risk of precipitated withdrawal— can initiate any time	QTc prolongation and Torsades de Pointes (TdP)	Metabolized primarily by CYP3A4; some metabolism by CYP2B6 and CYP2C19 (and CYP2C9 and CYP2D6 to lesser extent); see risk of toxicity and withdrawal for buprenorphine
N-methyl-D-aspartate receptor: antagonist	Less euphoria than illicit opioids	Respiratory depression; respiratory depressant effects peak later than analgesic effects	Caution when used with other central nervous system depressants (e.g., benzodiazepines)
Serotonin-norepinephrine reuptake inhibition	Limited data suggests safe in pregnancy	Fatal overdose if titrated too quickly	TdP risk is further increased if co-administered with other medications that prolong the QTc
	Analgesic effects (may need to split daily dosing to achieve consistent analgesia)	Hypotension	
		Must be obtained daily at licensed opioid treatment program	
Extended-Release Naltrexone			

MOR: competitive antagonist	Eliminates euphoric effects of other opioids	<p>Contraindicated in acute hepatitis or liver failure</p> <p>Precipitated withdrawal may occur if patient is not opioid free for a minimum of 7-10 days.</p> <p>Insufficient data to support safe use in pregnancy and lactation</p> <p>No analgesic effects; blocks analgesic effects of other opioids</p>	<p>Antagonizes effects of opioid-containing medicines including cough remedies and antidiarrheals</p> <p>No CYP p450 interactions</p>
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IN-HOSPITAL TREATMENT PROTOCOLS

1. In-Hospital MOUD Initiation and Continuation

Medications for opioid use disorder (MOUD) are effective in reducing morbidity and mortality from OUD (24). Although patients with OUD hospitalized for medical/surgical reasons represent a particularly high-risk group, it is known that inpatient MOUD initiation and maintenance on discharge improves inpatient treatment completion (e.g., of antibiotics for infection) and transition to outpatient care and decreases readmissions (25-27).

Despite the known efficacy of MOUD for OUD and the benefits of inpatient initiation of MOUD for those with OUD, most hospitalized inpatients with OUD do not receive optimal OUD management (28). Without effective treatment, there is risk of disruption along the spectrum of inpatient evidence-based care, including decreased opportunity for corrective treatments for endocarditis, increased discharges “against medical advice (AMA),” in-hospital and outpatient illicit drug use, and high mortality (29, 30).

An area of confusion exists about the legality of initiating and/or continuing methadone or buprenorphine maintenance for OUD during medical hospitalization. In the case of buprenorphine or buprenorphine/naloxone, any provider approved to prescribe buprenorphine for OUD, either via a filed Notice of Intent (NOI) for exemption for training through SAMHSA (31) or via a DATA2000 waiver, can both *initiate and maintain* buprenorphine monotherapy or buprenorphine/naloxone for a hospitalized patient with OUD.

Exceptions to federal regulations exist to allow for *continuation* of previously initiated MOUD by un-waivered prescribers and providers outside of “narcotic treatment programs.” These exceptions are based on carve outs (for “incidental to” reasons) in the federal regulations (Table 2) (32) allowing prescribers who are not authorized or waived to continue previously initiated methadone maintenance for OUD in hospitalized patients. This regulation was initially written when methadone was the only agent available for MOUD, but also applies to any opioid replacement therapy used for maintenance treatment for OUD (including buprenorphine and buprenorphine/naloxone).

Table 2. Title 21 Code of Federal Regulations PART 1306 – Prescriptions Part 1306.07 Administering or Dispensing of Narcotic Drugs (32)

A practitioner may administer or dispense directly (but not prescribe) a narcotic drug listed in any schedule to a narcotic dependent person for the purpose of maintenance or detoxification treatment if the practitioner meets both of the following conditions:

1. The practitioner is separately registered with DEA as a narcotic treatment program.
 2. The practitioner is in compliance with DEA regulations regarding treatment qualifications, security, records, and unsupervised use of the drugs pursuant to the Act.
- A.
- Nothing in this section shall prohibit a physician who is not specifically registered to conduct a narcotic treatment program from administering (but not prescribing) narcotic drugs to a person for the purpose of relieving acute withdrawal symptoms when necessary while arrangements are being made for referral for treatment. Not more than one day's medication may be administered to the person or for the person's use at one time. Such emergency treatment may be carried out for not more than three days and may not be renewed or extended.
- B.
- This section is not intended to impose any limitations on a physician or authorized hospital staff to administer or dispense narcotic drugs in a hospital to maintain or detoxify a person as an incidental adjunct to medical or surgical treatment of conditions other than addiction, or to administer or dispense narcotic drugs to persons with intractable pain in which no relief or cure is possible or none has been found after reasonable efforts.
- C.
- A practitioner may administer or dispense (including prescribe) any Schedule III, IV, or V narcotic drug approved by the Food and Drug Administration specifically for use in maintenance or detoxification treatment to a narcotic dependent person if the practitioner complies with the requirements of §1301.28 this chapter.

Initiation of MOUD in the Hospital Setting

Hospitalization can represent a critical opportunity to initiate evidence-based treatment for OUD (25, 33). Psychiatric and addiction consultation services can aid in the initiation and linkage to outpatient care for those with OUD (34, 35). For patients with OUD who are interested in and eligible for MOUD, the acute hospital setting provides a prime opportunity for engagement, treatment initiation, and connection with outpatient care. First, due to the high level of monitoring in the inpatient setting, aggressive use of non-medication support and adjunctive medications can assist the patient through withdrawal symptoms and successful induction. This is particularly helpful for patients at higher risk for complicated withdrawal, such as those on high-dose opioids, those on polypharmacy with other controlled substances, or those exposed to fentanyl. To that end, there has been an emerging literature on successful low-dose initiation of buprenorphine (currently known in the literature as micro-dosing), which is most easily accomplished in an inpatient setting. For patients with OUD who have rapidly come off prescription opioids, illicit opioids, or MOUD, whether inadvertently or for medical reasons, the inpatient setting also provides a safe environment for the 7-10 days of full withdrawal from opioids required to safely initiate XR naltrexone.

In-Hospital Buprenorphine Initiation

For patients eligible for and consenting to MOUD, buprenorphine initiation can be completed by an approved provider (NOI with SAMHSA completed or DATA 2000 waiver) during hospitalization. The traditional procedure requires the patient to enter a mild to moderate level of opioid withdrawal, which

can be measured using the Clinical Opiate Withdrawal Scale (COWS) (Table 3) (36). Ideally, the COWS score should be above 10, with a target range of 12-16 prior to induction with 2-8 mg sublingual buprenorphine. Repeated doses of 2-4 mg every 4 hours occur until the patient has neither cravings nor withdrawal symptoms. It can take more than 2-4 hours for some patients to reach the full effect of the medication (especially those patients on lower doses of prescription opioids for chronic pain). Those with injection drug use and moderate-severe OUD can often tolerate higher initiation doses of 8 mg. More aggressive protocols can be used in the hospital because of increased monitoring in the inpatient setting.

Table 3. The Clinical Opioid Withdrawal Scale (COWS) (36)

Resting Pulse Rate <i>Measured after patient is sitting/lying for one minute</i>		Runny nose or tearing <i>Not accounted for by cold symptoms or allergies</i>	
0	≤80 bpm	0	Not present
1	81-100 bpm	1	Nasal stuffiness or unusually moist eyes
2	101-120 bpm	2	Nose running or tearing
4	>120 bpm	4	Nose constantly running or tears streaming down cheeks
Sweating <i>Over past ½ hour, not accounted for by room temp or activity</i>		Gastrointestinal (GI) Upset <i>Over past ½ hour</i>	
0	No report of chills or flushing	0	No GI symptoms
1	One subjective report of chills or flushing	1	Stomach cramps
2	Flushed or observable moistness on face	2	Nausea or loose stools
3	Beads of sweat on brow or face	3	Vomiting or diarrhea
4	Sweat streaming off face	5	Multiple episodes of diarrhea or vomiting
Restlessness <i>Observation during assessment</i>		Tremor <i>Observation of outstretched hands</i>	
0	Able to sit still	0	No tremor
1	Report difficulty sitting still, but can do so	1	Tremor can be felt but not observed
3	Frequent shifting or extraneous movements of legs/arms	2	Slight tremor observable
5	Unable to sit still for more than a few seconds	4	Gross tremor or muscle twitching
Pupil Size		Anxiety or Irritability	
0	Pupils pinned or normal size for room light	0	None
1	Pupils possibly larger than normal for room light	1	Patient reports increasing irritability or anxiousness
2	Pupils moderately dilated	2	Patient obviously irritable, anxious
5	Pupils so dilated only rim of the iris is visible	4	Patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint Aches <i>Only pain attributed to opioid withdrawal is scored</i>		Yawning <i>Observation during assessment</i>	
0	Not present	0	No yawning
1	Mild diffuse discomfort	1	Yawning once or twice during assessment
2	Patient reports severe diffuse aching of joints/muscles	2	Yawning three or more times during assessment
4	Patient is rubbing joints or muscles and is unable to sit still because of discomfort	4	Yawning several times per minute

Gooseflesh Skin		Total Score and Severity of Withdrawal
0	Skin is smooth	5-12 = Mild
3	Piloerection of skin or arm hairs standing up	13-24 = Moderate
5	Prominent piloerection	25-36 = Moderately severe
		>36 = Severe

Switching from Methadone to Buprenorphine

Some patients may request to switch from methadone maintenance therapy to buprenorphine maintenance during a medical hospitalization. Several factors should be taken into account when deciding the best course of action, including coordination with the current MOUD provider; confirmation of current methadone dose and the patient’s stability on that dose, since transitioning from higher doses can be challenging during a short hospital stay and there is risk of instability; review of previous buprenorphine/naloxone trials and stability on those trials; exploration of overdose history; and the feasibility of the patient obtaining buprenorphine/naloxone as an outpatient. A risk/benefit analysis is necessary for the patient and provider to identify if the best course of action is to transition to buprenorphine. To make this transition to buprenorphine, patients ideally would be on a dose of 30 mg methadone or less to decrease the risk of precipitated withdrawal with traditional induction of 2-4 mg of buprenorphine (10). Buprenorphine micro-dosing procedures have shown anecdotal success in improving the transition for patients on higher doses of methadone. Given that buprenorphine is a partial agonist with high binding affinity to the μ -opioid receptor, it can potentially displace full-agonist opioids and precipitate withdrawal. Historically, to prevent precipitated withdrawal when undergoing buprenorphine induction, patients had to abstain from opioids for 12-24 hours for short-acting and 24-72 for long-acting full-agonist opioids. Abstinence from opioids is an identified limitation of buprenorphine induction because for many patients, abstinence is not feasible due to distress of severe withdrawal symptoms and exacerbation of severe pain (37). This occurs not infrequently in hospital settings when patients are admitted with an acute medical condition requiring pain management or an acute surgical problem requiring post-operative pain management.

Buprenorphine Low Dose Initiation (Micro-dosing)

Buprenorphine micro-dosing is a novel approach to buprenorphine induction that entails starting very small initial doses of buprenorphine while concomitantly continuing to give full- μ -agonist opioids. This approach eliminates the need for abstinence prior to initiation of buprenorphine. The daily dose of buprenorphine is incrementally increased to a therapeutic dose and the full-agonist opioids are weaned and discontinued once the patient is comfortable on buprenorphine (38). Of note, the “micro-dosing” nomenclature technically refers to use of microgram doses of buprenorphine, but that is not always the dosing scale used with low-dose initiation. Since the “micro-dosing” terminology is used extensively in the literature, we have used it interchangeably with “low-dose initiation” in this document.

Currently there are two different approaches to low-dose initiation. The first method involves applying a transdermal buprenorphine patch (20 mcg/hr, 15 mcg/hr, 10 mcg/hr, or 5 mcg/hr, dependent on MME) and then waiting 48 hours prior to initiating small doses of buprenorphine SL (1 mg TID). The patch can be tapered after 2-3 days and should be discontinued after 5 days. The second approach, known as the “Bernese Method” (39), does not use a buprenorphine patch, but rather immediately initiates small doses of SL buprenorphine (0.125-0.5 mg). Most patients tend to tolerate low-dose initiation with minimal withdrawal symptoms or cravings.

Currently, there are case reports but no randomized controlled studies of micro-dosing in the literature. Case reports have suggested that micro-dosing may be helpful in patients with illicit opioid use, including fentanyl, in the outpatient setting.

XR Naltrexone Initiation in Hospitalized Settings

For hospitalized patients with OUD who have been off opioid agonists for 7-10 days, XR naltrexone initiation is an option for OUD. After opioid withdrawal has been completed, outcomes for OUD are similar for patients maintained on XR naltrexone as compared with buprenorphine (40). Prior to receiving the XR naltrexone injection, patients receive a test dose of oral naltrexone to ensure they do not go into withdrawal.

Continuation of MOUD in the Hospital Setting

When continuing methadone or buprenorphine for hospitalized patients, the most important first step is to coordinate with the prescription drug monitoring program and the patient's outpatient provider to determine current dose. In general, methadone or buprenorphine should be continued at the confirmed outpatient maintenance dose. For patients taking methadone, coordination with the opioid treatment program to identify current methadone dose and date and time of last dose given is essential; dosing of methadone distributed from opioid treatment programs will not be visible through state prescription monitoring programs. If the home dose cannot be immediately verified, a low dose of 10-30 mg typically is considered safe. When determining inpatient dose, it is also important to consider the patient's current medical conditions (including sleep apnea), medical stability, and state of alertness, as well as any potential drug-drug or drug-illness interactions for which the patient may be at risk.

Overdose Education and Naloxone Distribution (OEND) for Hospitalized Patients

For individuals at high risk for opioid overdose, especially those with OUD who decline or cannot access MOUD or who are being discharged with decreased opioid tolerance, hospitalization represents an important opportunity for providing overdose education as well as naloxone education, prescription, and/or distribution, especially for those who may not otherwise receive such an intervention (41). There are various methods by which to make naloxone available to an individual: a prescription can be given for the patient to fill at a pharmacy after discharge; an individual can be referred to a "community distributor" who may be able to directly dispense naloxone at no charge to the patient; or the hospital staff may be able to dispense naloxone directly to an at-risk patient. Of note, hospital regulations exist about *dispensing* medications, including naloxone, directly to an individual, and it may be required that the hospital have a dedicated protocol, have a standing prescription, and/or be registered as a "community distributor" to receive and dispense naloxone kits directly to patients (41). State policies vary on these regulations and need to be checked prior to initiating a naloxone *distribution* service from a hospital-based setting.

2. Perioperative Management of Patients with OUD

Acute and Perioperative Pain Management

As part of the response to the opioid crisis, there is a rising number of patients maintained on MOUD with long-acting partial μ -receptor agonists like buprenorphine or full μ -opioid agonists such as methadone. This can pose challenges for perioperative and acute pain management. Patients with OUD (and those physically dependent on opioids, including MOUD) are at risk for having greater difficulty with pain management, including increased pain sensitivity and decreased pain threshold. This can lead to lowered pain tolerance (42) resulting in higher opioid analgesic requirements (up to 1.5 times higher than non-tolerant individuals) and more frequent interval dosing due to opioid cross-tolerance. Some literature suggests that surgical patients on chronic opioid agonists for OUD or cancer and non-cancer

pain use on average 3 times higher MME in the first 24 hours after surgical procedures as compared to opioid-naïve matched controls (43).

Despite the increased frequency with which patients maintained on MOUD are being managed for acute and/or peri-operative pain, there is a lack of rigorous evidence to guide clinicians in the acute or peri-operative management of individuals maintained on MOUD. With varied approaches based on the anticipated “painfulness” of a planned surgery and the preferences of the surgical and anesthesia teams, patients can face inconsistent approaches, stigma, and under-treatment of pain (44, 45). Social determinants that may contribute to under-treatment of pain include race, ethnicity, English proficiency, and gender, among others (46-52). Approaches to management are generally based on which maintenance medication a patient is prescribed and the urgency of the procedure. With increased experience and exposure, clinicians are gaining valuable insight and advocating for innovative approaches such as enhanced recovery after surgery to provide a framework to ensure high-quality peri-operative and acute care for opioid-tolerant patients, including those on MOUD with buprenorphine or methadone (53).

A basic premise of the effectiveness of chronic administration of partial μ -opioid agonists (buprenorphine) and μ -opioid agonists (methadone) for OUD treatment is induction of cross-tolerance to other opioids such as heroin. This premise, combined with the high μ -opioid receptor affinity of buprenorphine (which can cause displacement of other opioids at the μ -opioid receptor, as in precipitated opioid withdrawal), has led to debate on the following questions, mostly for buprenorphine-maintained patients: 1. Does being maintained on opioid agonists/partial-agonists peri-operatively limit opioid analgesia in the peri-operative or acute pain settings, leading to inadequately controlled pain? 2. Can a decrease in or discontinuation of buprenorphine increase μ -opioid receptor occupancy and increase peri-operative or acute pain opioid analgesia? There is no uniformly accepted treatment guideline that addresses continuation of buprenorphine or methadone in the perioperative period (54), and randomized controlled trials are needed. A clinical practice advisory by the Perioperative Pain and Addiction Interdisciplinary Network (55), and a number of recently developed institutional protocols (56-59), suggest continuation of buprenorphine or methadone at currently prescribed doses for most patients peri-operatively (including the day of surgery) or during episodes of acute pain.

Pre-, intra-, and post-operatively, and for acute pain, multiple guidelines (7, 10), consensus statements (55, 60), and authors (53, 61) recommend use of non-opioid multi-modal analgesia for patients receiving long-term opioid therapy like buprenorphine or methadone. Approaches that can reduce opioid use and decrease post-operative pain include the use of acetaminophen, NSAIDs, gabapentin/pregabalin, dexamethasone, lidocaine, ketamine, magnesium, dexmedetomidine, esmolol, mindfulness relaxation training, and regional anesthesia when possible (61). Post-operatively, if pain control is inadequate with non-opioid multi-modal approaches, it is suggested to add full μ -opioid agonists with higher μ -opioid receptor affinity, such as fentanyl or hydromorphone, to buprenorphine or methadone (10, 54, 62, 63). This requires acknowledgment of the possible need for increased opioid doses to overcome opioid tolerance and the high receptor occupancy of buprenorphine to achieve adequate analgesia (37-39). Whenever adding opioids to other opioids, close monitoring for sedation is recommended (64). Opioid analgesics with antagonist properties (nalbuphine, butorphanol) are not recommended in patients receiving buprenorphine or methadone, as they may precipitate acute withdrawal (14, 17, 65-67). Collaborative discussions with the surgeon, the anesthesiologist, addiction specialists, primary care, the patient, and the patient’s family are essential both peri-operatively and near-discharge (59, 68). Given the differences that can occur both in the pain experience and analgesia in those with OUD and in those

maintained on chronic opioid agonists, good communication and coordination of care can optimize delivery of safe, compassionate care that decreases the risk of undertreating pain while being mindful of comanagement of SUD.

Buprenorphine

There is a lack of consensus on perioperative management of patients treated with MOUD. Several approaches for perioperative buprenorphine management have been suggested, with limited evidence to support any approach (69). Historically, buprenorphine was discontinued prior to surgery due to the concern that additional opioids may be less effective in the presence of buprenorphine, which has a high binding affinity to the μ -opioid receptor (61, 69). In the absence of buprenorphine, μ -opioid receptors will be available to be filled by another opioid. This shift of available receptors may lead to over- and/or under-dosing of pain medication. Reinduction of buprenorphine in the immediate post-operative period may prolong hospital stays (61). Ultimately, stopping buprenorphine in a patient with stabilized OUD may lead to discomfort and increase the potential for relapse. More recent literature suggests that patients who continue home buprenorphine maintenance dose (or a slightly lower dose) have lower opioid patient-controlled anesthesia (PCA) requirements than those whose home dose has been discontinued (69, 70).

Some reports have shown success with increasing buprenorphine as the primary opioid analgesic as well as dividing the daily dose into 8-hour intervals to optimize analgesic coverage (54, 61, 62). If inadequate acute or peri-operative pain control is still experienced with the use of multi-modal therapy and full μ -opioid agonists, there may be consideration of buprenorphine dose reduction to 8-12 mg to increase μ -opioid receptor availability for other full-agonist opioid analgesics (55, 71, 72). Theoretically, a buprenorphine maintenance dose reduction liberates opioid receptors for full opioid μ -agonists to bind, allowing for adequate pain control without the need to fully discontinue buprenorphine. The literature suggests that tapering buprenorphine to a dose of 8-12 mg sublingually permits sufficient μ -receptor binding availability (69, 72-75). No prospective studies have compared efficacy of continuing a patient's home buprenorphine dose to efficacy of decreasing the dose to provide increased μ -opioid receptor availability.

It is important to be aware that some hospitals will transition patients maintained on a buprenorphine/naloxone product (e.g., Suboxone, Zubsolv) to a buprenorphine mono-product (e.g., Subutex, buprenorphine without naloxone), generally for cost-efficiency reasons. This is an acceptable practice given that naloxone is present in the combination product solely to prevent injection of buprenorphine, which would be unlikely, though not impossible, during hospitalization. Given the very limited bioavailability of naloxone when taken sublingually, concerns about continuing buprenorphine/naloxone peri-operatively due to the presence of naloxone are not practically significant, as naloxone SL should not interfere with μ -opioid receptor occupancy. There is no research currently on the newer, longer-acting injectable formulations of buprenorphine in the peri-operative period or acute pain setting.

For those individuals unable to use SL or oral medications peri-operatively, IV buprenorphine is available. Butrans patches are FDA-indicated for pain but not for OUD, and are typically expensive and not covered by insurance.

Methadone

Although most recent attention has been given to patients maintained on buprenorphine MOUD formulations, very low-level evidence suggests that for those maintained on methadone, additional

methadone for pain management may be an effective analgesic approach with appropriate consideration for risks such as QT prolongation and sedation (42). Because the analgesic duration of action is thought to be about 8 hours for methadone, dividing the total methadone dose into 8-hour increments should, in theory, provide improved pain control (76), although this has not been formally studied. Importantly, it has been shown that opioid analgesic medications can be safely used for post-surgical pain in patients on methadone maintenance therapy without increasing risk of relapse (77).

For patients unable to take oral medications in the peri-operative setting, IV methadone is available. The dose conversion from enteral to IV methadone is poorly defined, and can be difficult at higher doses, with most recent evidence suggesting oral dose reduction of 30% (78). Typically, the total daily dose is divided into smaller doses every 6-8 hours to provide optimal pain control. Furthermore, the preservative in IV methadone, chlorobutanol, acts synergistically with methadone to prolong the QTc interval (79), thus increasing the risk for Torsades de Pointes (TdP). Close monitoring and consultation with a pharmacist are advised.

When utilizing methadone for peri-operative analgesia, it is important to follow the same monitoring parameters as for any use of methadone. Methadone can prolong the QTc; if the QTc is greater than 500 msec, consider reducing or holding QTc prolonging medications, including methadone, to decrease the risk of TdP (80). In addition, methadone can result in oversedation and respiratory depression whether used alone, in combination with other sedating medications, or in the context of acute illness. In these situations, continuation of methadone with close monitoring is advised (81). Methadone should also be used with caution in patients with decompensated liver disease. It is important to regularly monitor transaminase levels and pay close attention to all coadministered medications that may induce or inhibit the hepatic metabolism of methadone via the cytochrome p450 system (81).

Naltrexone

Naltrexone is a full opioid antagonist and can limit the effects of opioids. Guidance for peri-operative management of patients maintained on XR naltrexone is based on case reports and pharmacokinetic studies. For elective surgeries, patients and providers must consider the risks and benefits of the elective surgery and assess the anticipated need for post-operative opioid analgesia vs. the ability to manage post-operative pain using non-opioid techniques. Extended-release injectable naltrexone is active for 28 days (peaking at 7 days), and the antagonist effects decrease over the course of the month. There are no currently published data demonstrating exactly when opioid antagonism can be overcome, but reports have demonstrated absent analgesia in the first 2 weeks of treatment (82) and successful pain management starting in the 4th week of treatment (83). Delaying surgery for 4 weeks to allow for complete naltrexone washout prior to elective surgery is ideal, though opioid management after chronic opioid antagonism can still be unpredictable, with the possibility of either attenuation or enhancement of opioid responsiveness (61, 84). Like management of individuals on other forms of MOUD, post-operative management for patients maintained on chronic naltrexone should include multimodal non-opioid approaches (53, 55, 60, 61, 85), but unlike with the other forms of MOUD, individuals previously maintained on XR naltrexone should be introduced to post-operative opioids as needed, as though they were opioid-naïve, with close monitoring for adverse events (74, 85). Unplanned surgeries and acute pain cannot take advantage of such foresight for a planned 4-week washout, and animal studies have shown that to overcome opioid receptor antagonism, opioid doses may need to be increased 10-20 times the usual clinical dose to achieve analgesia (86). Reported experience overcoming naltrexone blockade in humans is very limited (87, 88).

Current clinical practice for patients prescribed oral naltrexone for maintenance therapy undergoing elective procedures includes discontinuation 72 hours (accounting for five half-lives) prior to scheduled procedure (61). For those patients receiving IM naltrexone, discontinuation for at least 30 days (89) prior to elective procedure is ideal. For emergency procedures or need for acute pain management (e.g., motor vehicle accident), clinicians may discontinue naltrexone on presentation and consider regional anesthesia, conscious sedation, or general anesthesia (89). Naltrexone may be resumed once additional opioids are no longer needed. It can be restarted post-procedure or initiated after a period of abstinence from opioids for a minimum of 7-10 days (90).

Key Points About Perioperative Management

- Prospective research in this area is needed to test anecdotal experience and measure outcomes for different peri-operative approaches to individuals treated with MOUD.
- Current practice favors continuation of home dose buprenorphine and methadone in the peri-operative and acute pain settings with consideration of decreased dosing in certain circumstances.
- Consider multimodal non-opioid analgesia for patients treated with long-term MOUD when in the peri-operative setting.
- Collaboration between surgery, anesthesia, primary care, SUD-specialists, patient, and family is essential for safe, compassionate care.

TRANSITIONS OF CARE

Transition points in care, such as hospital discharges, provide important opportunities to engage patients in short- and long-term outpatient treatment. This section will review several models used in the process of connecting patients from inpatient hospitalization to community-based treatment.

1. Bridge Clinics

In providing medication treatment for patients with OUD during their hospitalization, the critical next step is to ensure the successful transition of care to ongoing treatment in the community, i.e., linkage. Unfortunately, transition of care represents a risky time for many hospitalized patients due to the difficulties inherent in arranging suitable and timely follow-up appointments. Poor linkage after hospitalization is likely due to many factors, but it contributes to poor outcomes, including avoidable readmissions (91). Studies of patients initiated on buprenorphine during medical hospitalization have suggested that linkage to outpatient treatment also remains a major challenge, with rates generally at around 50% (35, 92). For example, Englander and colleagues implemented a robust hospital-based addiction medicine consult service to facilitate buprenorphine initiation as well as linkage to aftercare (93). Thirty-eight percent of those receiving this intervention successfully linked with ongoing addiction treatment following discharge, compared to 23% among matched controls who did not receive the intervention. This suggests that initiation of medication treatment alone is insufficient to ensure adequate linkage with aftercare.

The rates drop further if patients receive buprenorphine without any bridging prescription. In a randomized trial of 145 hospitalized patients, 72% of those randomized to receive a buprenorphine prescription to continue treatment in the community had successful linkage, compared to 12% of those who only received a short course of buprenorphine for detox purposes (25). The high linkage rate in this study in those who received a prescription at discharge may have been due to referral of the study participants to the hospitals' own buprenorphine treatment program.

In a study by D'Onofrio and colleagues, emergency department (ED) patients with OUD were randomly assigned to receiving referral to treatment, to receiving brief intervention and referral, or to being initiated on buprenorphine and referred to a local primary care clinic to continue treatment (94). Remarkably, 78% of those randomized to receive buprenorphine successfully linked to ongoing treatment, as compared to 37% for those receiving a referral and 45% for those receiving additional brief counseling. The high linkage rate in this study, like that in the study by Liebschutz and colleagues (25), may have been due to the availability of the primary care clinic at the same hospital to guarantee an intake within 72 hours of the ED visit to continue the buprenorphine treatment. Indeed, the study procedures specified that the primary care clinic would be responsible for treating the patients for up to 10 weeks, at which point patients were transferred to other programs or clinicians in the community. The success of this time-limited treatment, offered with minimal barriers to entry, served as the catalyst to further implement such "bridge clinics" targeting patients with OUD in acute medical settings.

The ability of such bridge clinics to offer an intake visit with little or no notice and avoid any disruptions to buprenorphine treatment therefore may be important to ensuring continuity of treatment following discharge. This approach contrasts with traditional addiction treatment models in which visits are typically scheduled days or weeks in advance, and prescriptions for buprenorphine are usually not offered on the first visit. Studies to date make it clear that for patients with OUD who are being discharged from acute care facilities, this delay places them at risk for relapse due to disruptions in their treatment.

The bridge-treatment model may include the harm reduction approach, in which there is a prioritization of treatment engagement over abstinence or adherence to appointments, counseling, or 12-step meetings (95). Provision of peer recovery services, and efforts to address social determinants of health, may also play a significant role. Other types of low-barrier methods may even employ a mobile van service so treatment can be offered at locations most convenient for the patient (96). Bridge clinic models may not be suitable for all patients, however, as some may benefit from more structured programs or opioid treatment programs. This highlights the need to individualize treatment plans for different patients, and that a range of services is still needed to meet the needs of patients being discharged from the hospital.

2. Inpatient Psychiatry

For those hospitalized on psychiatric units where suicide risk is often the primary reason for admission, MOUD is of critical importance. Persons with OUD are at increased risk of depression, suicidal ideation, suicide, and unintentional overdose (97). MOUD reduces the risk of overdose and all-cause mortality (98). Preliminary evidence suggests that buprenorphine relieves depressed mood and suicidal behaviors in those with major depression and treatment-resistant depression (99). Psychiatrists can administer buprenorphine or methadone to treat OUD as an adjunct to inpatient treatment for mood disorder or psychosis (32). Despite this, psychiatric inpatient units more commonly provide opioid withdrawal management and defer initiation of MOUD until after hospital discharge, creating an unnecessary risk of opioid relapse and overdose. Many of the barriers to initiating MOUD in the general

hospital likely apply to acute psychiatric inpatient units as well, although no studies currently exist that examine barriers and facilitators to initiating MOUD during psychiatric hospitalization. Given the association of OUD with suicide and the potential for MOUD to alleviate depressed mood and to reduce suicide risk and opioid overdose, more research is urgently needed to determine barriers and facilitators to initiating MOUD during psychiatric hospitalization and the optimal treatment approaches to reduce risk of suicide and all-cause mortality in this high-risk population (100). As with discharge from medical hospitals, continuity of care following psychiatric admission is of critical importance.

3. Outpatient Parenteral Antimicrobial Therapy

Outpatient parenteral antimicrobial therapy (OPAT) is the practice of monitored administration of parenteral antimicrobials for patients with complex infections outside of the hospital setting, usually in a rehabilitation facility, an infusion center, or the home. For individuals with serious infections that are not due to injection drug use (IDU), OPAT is routinely offered and is the standard of care for endocarditis not due to IDU. Individuals with a history of OUD, however, are routinely excluded from OPAT consideration due to the perception that the individual will inevitably use the catheter to inject drugs (101). Other cited barriers include unstable housing, unreliable transportation, unwillingness of an infectious disease physician to follow as outpatient, risk of incomplete course of antimicrobials, risk of being sued, inadequate Medicare coverage if non-homebound, and lack of existing models (102, 103). The 2018 Guidelines of the Infectious Disease Society of America on use of OPAT in people who inject drugs (PWID) declined to make a recommendation about whether PWID can use OPAT at home, emphasizing the importance of a case-by-case evaluation (104). However, while barriers may be of real concern, the available evidence suggests that outcomes for OPAT among individuals who inject drugs are generally comparable to outcomes of those who do not inject drugs. A recent literature review indicated that antibiotic completion rates, mortality, and catheter complication rates were comparable between those who do and do not inject drugs (105). Subsequent reports have also indicated that outcomes with injection drug users on OPAT are indeed excellent, with considerable cost savings that may be realized through reduced days spent in acute or sub-acute care facilities (106). A study of patients receiving OPAT found no differences in line manipulation or secondary bacteremia between housed PWID and housed non-PWID patients who remained engaged in treatment. Notably, non-housed PWID had a significant increase of line manipulation and secondary bacteremia, suggesting that housing status plays a role in OPAT success (107).

A 9-point risk assessment tool was developed to stratify risk of OPAT in PWID who require intravenous antibiotics and categorizes patients as mild, moderate, or high risk (108). Mild-risk cases are discharged for the duration of IV antibiotics with outpatient addiction care, whereas moderate- and high-risk cases are kept in the hospital for the duration of IV antibiotic treatment. A comparison of patients treated pre-initiation of the tool (n=37) vs. post-initiation (n=100) demonstrated a post-intervention reduction of hospital costs by 33%, reduced hospital length of stay (LOS), and increased capacity for 333 additional patients. These results suggest that prioritization of higher-risk patients who will require resource-intensive admissions ultimately reduces cost and decreases LOS (109). Proposed criteria and conditions for successful home-based OPAT include optimization of treatment for SUD while hospitalized, collaboration between addiction and infectious disease specialists, use of a care navigator or case manager to facilitate transition to outpatient care, safe and stable housing, and willingness of patient to engage in close addiction and infectious disease (ID) follow-up (102). Notably, observations from the SARS-CoV-2 pandemic reveal that home-based OPAT may be a more attractive option than before, given new infection control risks at nursing and rehabilitation facilities (102).

Not all hospital systems will have the resources to provide OPAT to individuals with OUD, and some hospitals may need to keep the patient hospitalized for the entire duration of the intravenous antibiotics. Others will continue to rely on sub-acute treatment facilities to continue the intravenous antibiotic therapy. Unfortunately, skilled nursing facilities have routinely rejected patients with OUD from being admitted even if the patient has been stable or recently initiated on MOUD (110). Stigma likely plays a role in this practice, but facilities also must navigate the complex regulatory requirements that hinder their ability to fully understand the options available. For instance, patients on stable methadone treatment can continue to receive their doses by visiting their program daily. Alternatively, the methadone program can transfer the methadone to the facility with the appropriate regulatory approvals. For those patients who have not yet initiated methadone maintenance treatment, current law prohibits the initiation of methadone maintenance at skilled nursing facilities (111). Patients receiving buprenorphine treatment should be able to receive the medication like any other home medication. If the patient was initiated on buprenorphine during the hospital stay and therefore has no outpatient prescriber, the facility would need a buprenorphine-waivered provider to prescribe the medication.

4. Patient Navigation

Given that addiction treatment in the community setting is often fragmented from that in hospital systems, even experienced clinicians can struggle to navigate the addiction treatments available to patients. Worse, patients and families certainly struggle to navigate the confusing landscape. From understanding the levels of care needed and finding a suitable therapist or provider or 12-step meetings, there is a myriad of options that often needs to be considered. Given that most hospitals do not have the resources to launch a bridge clinic, additional approaches may be needed for hospital systems to help patients navigate post-hospital treatment options. Some hospitals have incorporated interventions to support patient navigation through the addiction consult services, recovery coaches, or patient navigators. For example, Nordeck and colleagues reported on the implementation of an addiction C-L service that was composed of a multidisciplinary team including social workers (112). The team made frequent referrals for follow-up care with community programs upon discharge from the hospital. The results indicated that patients with OUD had the highest readmission rates, suggesting the elevated risk for ongoing medical issues that patients with OUD face following discharge.

In another study, Liebling and colleagues report on a program that employed peer recovery specialists and patient navigators to target hospitalized individuals with SUDs (113). Peers, who were individuals with at least 4 years of recovery, were available to engage with patients on short notice by being on call 24/7 to patients in emergency rooms or inpatient settings across 20 hospitals. The peers then provided an initial bedside consultation followed by regular checkups by phone or in person for several months after discharge. If interested, patients could then be referred to a patient navigator, a bachelor's level clinician with at least 3 years of experience treating patients with SUDs, to provide case management and referrals to treatment programs. The program results showed that most patients accepted the meeting with the peers, and about 40% of those individuals also accepted a referral to the patient navigator. These findings suggest that hospitals may need to consider these additional approaches to help patients with OUD navigate after-care plans in order to facilitate linkage to ongoing treatment. Regardless of the options considered, creating an ongoing partnership and relationship with community programs that treat SUDs will facilitate the referral process in the longer term.

SPECIALTY-SPECIFIC CONSIDERATIONS

1. Infectious Disease

Hospitalists, internists, and ID, cardiology, and surgery specialists often encounter patients with OUD who present with blood-borne infections transmitted via IDU, including infectious endocarditis (IE), cellulitis, osteomyelitis, septic arthritis, epidural abscess, human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV), among others. A recent review of public health data sources examining IDU-related infection syndromes estimated a prevalence of at least 100,000 cases of skin and soft tissue infections and an incidence of thousands of episodes of IE annually in the United States (114). The rise in IDU-infection-related hospitalizations (115, 116) has resulted in a significant increase in hospitalization costs even when accounting for inflation. From 2002 to 2012, the total inpatient charges for OUD-related infection increased from approximately \$190 million to \$700 million, with an estimated charge per hospitalization of approximately \$100,000 (115).

Parenteral Antibiotics

Serious infections including bacteremia and endocarditis frequently require treatment with intravenous antibiotics. The need for weeks-long parenteral antimicrobial therapy in the inpatient setting can be a barrier to completion of treatment for many patients with OUD. As many as 30% of persons who inject drugs (PWID) leave the hospital prematurely as a patient-directed discharge (i.e., discharge “against medical advice/AMA”) (117), often without linkage to outpatient SUD treatment and without resources to complete antibiotic treatment. Risk factors for non-completion of therapy and patient-directed discharge include stigma and negative interactions with staff, poorly controlled cravings and withdrawal symptoms, poorly controlled pain, restrictive hospital policies that are carceral in nature (e.g., restricting mobility or 1:1 observation), use of illicit drugs in the hospital, and outside psychosocial obligations (118).

Transition to Oral Antibiotics

There is growing evidence that transitioning from parenteral to oral antibiotics is non-inferior to continued intravenous (IV) antibiotics for osteomyelitis and endocarditis (119), suggesting that oral antibiotics may be a viable treatment option for PWID with invasive infections who are at risk of treatment non-completion. A retrospective chart review of 293 PWID admitted for invasive infections compared 90-day readmission rates for patients who completed a full course of inpatient IV antibiotic therapy, patients who partially completed inpatient IV antibiotics (mean LOS 14.5 days) and received an oral antibiotic prescription at the time of patient directed discharge, and patients who partially completed inpatient IV antibiotics (mean LOS 12.5 days) and did not receive an oral antibiotic prescription at the time of discharge. Patients who received oral antibiotics had similar readmission rates to patients who completed a full course of inpatient IV antibiotics. The absolute risk reduction of 90-day readmission for partial IV/partial oral antibiotic therapy compared to no oral antibiotic therapy was 35.7%, with a number needed-to-treat of 3 (120). These data support the approach of using oral antibiotic therapy in PWID when parenteral antimicrobials cannot be used.

Long-Acting Parenteral Antibiotics

In patients for whom neither OPAT nor oral antibiotics are options, long-acting lipoglycopeptide (LAL) antibiotic infusions may be an alternative treatment. Dalbavancin (121) and oritavancin (122) are broad-spectrum LAL antibiotics that act against gram-positive bacteria, provide prolonged tissue exposure with long half-lives (200-300 hours and 346 hours, respectively), have large volumes of distribution with high protein binding, and have response rates comparable to those of standard antibiotic agents for acute bacterial skin and skin structure infections. Dalbavancin is administered as a one- or two-time 1500 mg or 1000 mg +500 mg 30-minute IV infusion (121). Oritavancin is administered as a one-time 3-hour 1200 mg IV infusion (122). There is growing evidence for other off-label indications, including osteomyelitis, prosthetic joint infections, bacteremia, and endocarditis (123, 124).

A retrospective cohort analysis of 24 cases of infection in 23 PWID treated with at least one course of oritavancin for endocarditis, bone/joint infection, bacteremia, or skin/soft tissue infection found that of the 24 cases, 19 (79%) achieved clinical cure, three (13%) failed treatment, and two (8%) were lost to follow-up. Of these 23 subjects, 16 were homeless at the time. This study suggests that the LALs are an important new consideration for PWID who are being treated for complex gram-positive infections, including those with housing insecurity (125).

Clinicians should be aware that oritavancin is a weak inhibitor of CYP2C9 and CYP2C19 and an inducer of CYP3A4 and CYP2D6 (122). Buprenorphine (a substrate of CYP3A4) concentrations may be reduced if administered concurrently. As methadone is metabolized by all four of these isoenzymes, patients should be monitored for signs of both toxicity and lack of efficacy when it is used with oritavancin. There is minimal potential for drug-drug interactions with dalbavancin (121).

Commonly Encountered Infections

Infective Endocarditis (IE)

IE is an infection of the heart valves and/or endocardium caused by bacteria entering the bloodstream from a variety of sources, including dental procedures, cardiac implantable electronic devices, chronic skin disorders, burns, and IDU. Infective endocarditis is a common complication of IDU that accounts for an increasing percentage of the mortality and health care cost associated with OUD (115,126).

Mechanisms by which IDU increases risk of IE include direct injury from particulate matter, use of contaminated equipment and non-sterile injection techniques, and direct cardiac physiologic effects including vasospasm and cardiac injury (127-131). Sixteen percent of IE in North America is due to IDU (132). The incidence of injection drug use-related IE (IDU-IE) in PWID is 1.5 to 4 cases per 1,000 years of IDU (133). Surgical intervention (usually valve repair or replacement) is required in 20-40% of IDU-IE patients at the time of first episode IE. More than half of these patients will require repeat surgical intervention due to ongoing IDU (134). Types of injected drugs vary regionally, but in general, opioids account for most patients with IDU-IE (67%), followed by methamphetamine (26.3%), bath salts (5.3%), and cocaine (16%), with the remainder unknown (133).

IE often results in prolonged hospitalizations and rehospitalization due to lengthy treatment with parenteral antibiotics, surgical valve repair or replacement, and recurrence (135, 136). Comparison of outcomes of non-IDU-IE (n=96,344) to IDU-IE (n=27,432) from the National Readmissions Database demonstrated increased IDU-IE from 15.3% to 29.1% of all IE cases between 2010 and 2015.

Furthermore, LOS and readmission rates for IE recurrence, septicemia, and drug abuse were all significantly higher in patients with IDU-IE (136).

Optimal management of IDU-IE requires collaboration among cardiology, cardiac surgery, and psychiatry/addictions with a dual focus on the infection and the SUD. The American College of Cardiology (ACC)/American Heart Association (AHA) guidelines for management of patients with valvular heart disease recommend consultation with addiction medicine “to discuss the long-term prognosis for the patient’s refraining from actions that risk infection before repeat surgical intervention is considered” (137). It is notable that the ACC/AHA guidelines do not comment on provision of SUD treatment for patients with IDU-IE, perhaps for the same reasons that psychiatry has not more actively owned this, including lack of training and knowledge (138), misperceptions about feasibility of initiating MOUD in the hospital (139), lack of outpatient MOUD prescribing resources (140), and ongoing stigma. Notably, policies requiring abstinence as a requirement for surgery, including the use of signed contracts (141), are ineffective, especially during the critical period of acute IE when management of substance

withdrawal may not be prioritized. The expectation that a written agreement will compel abstinence fails to consider the neurobiology of SUDs, comorbid psychiatric illness, and complex psychosocial conditions, and not so subtly promulgates disparate medical treatment for patients diagnosed with an SUD (142). Furthermore, the position that surgical treatment of endocarditis in PWID is futile or wastes resources is incomplete when, in most cases, the underlying OUD has not been treated (103). A retrospective cohort study of 768 subjects with OUD hospitalized with IE found that patients who had received MOUD (primarily naloxone and buprenorphine) within 30 days of discharge had a lower opioid-related overdose rate and lower 1-year rehospitalization rate than did patients who had not received MOUD (143).

Human Immunodeficiency Virus and Hepatitis C Virus

Sharing of equipment by PWID increases the risk of infection with HIV, HCV, soft tissue infection, and IE (144). From 2007 to 2017, though the overall incidence of IE remained stable, it increased significantly in young persons (aged 18-29 years) with HCV (estimated annual percentage change [EAPC] 16.3) and OUD (EAPC 14.8) (145). The rise of IE in persons with HCV infection and OUD likely reflects recent trends, including a near five-fold increase of reported cases of acute HCV between 2010 and 2019, with an estimated 57,500 new HCV infections in 2019 (146).

From 2007 to 2017, the incidence of IE decreased in persons living with HIV (145). IDU is now the most common risk factor for acquiring HIV, whereas most persons diagnosed with HIV in earlier years acquired it through sexual behaviors. Notably, there have been several recent outbreaks of HIV in PWID, specifically in young, White, rural populations without access to syringe services programs (SSP) or MOUD (147). The provision of MOUD with opioid agonists to persons living with HIV (PLH) has a significant positive impact on receipt and adherence with antiretroviral treatment (ART), HIV viral suppression, HIV transmission, and use of illicit opioids (148-150). A meta-analysis of the association between opioid agonist therapy and HIV incidence demonstrated a 54% reduction of new HIV infections with use of MOUD (150).

When prescribing MOUD to PLH it is essential to consider pharmacokinetics, specifically drug-drug interactions between ART and MOUD. Efavirenz (CYP3A4) is a cytochrome p450 inducer of methadone metabolism, so higher dosing of methadone may be required for patients taking this medication. Ritonavir is both an inhibitor of CYP3A4 and CYP2D6 and an inducer of CYP2C19 and CYP2C9, all of which metabolize methadone. As a result, methadone concentrations may be increased or decreased and should prompt monitoring for both respiratory depression and sedation as well as opioid withdrawal. Conversely, methadone increases zidovudine levels by reducing renal clearance (151, 152). Buprenorphine has few drug-drug interactions with ART.

A trial of PLH randomized to clinic-based buprenorphine vs. referral for methadone maintenance found that patients taking buprenorphine were more likely to engage in treatment for OUD. However, there were no differences in receipt of ART, HIV viral load, or CD4 counts (153). Oral and extended-release naltrexone have been shown to have positive safety profiles in PLH, each with minimal hepatotoxicity (148, 154, 155) and no effect on cytochrome P450 metabolism.

Harm Reduction and MOUD

IE, HIV, HCV, HBV, and other infections can be prevented through implementation of harm reduction strategies (156) and MOUD. Harm reduction interventions include SSPs that provide access to clean injection equipment (sterile syringes, needles, water, filters, cookers), fentanyl test strips, alcohol swabs, products for hand hygiene, and syringe cleaning (bleach). SSPs can be a convenient setting for clinical

engagement and other harm reduction services like MOUD, HIV pre-exposure prophylaxis (PrEP), education about infection prevention, and treatment of minor infections (145).

The Harm Reduction Coalition Safety Manual for Injection Drug Users “Getting Off Right” (157) is a comprehensive and high-yield resource for both PWID and the clinicians treating them. This how-to guide provides instructions for PWID on safest practices for choosing materials, drug preparation, injection techniques, and management of health complications and overdose. The Harm Reduction Coalition website also includes useful resources with links to directories for SSPs, naloxone distribution, and local buprenorphine providers through SAMHSA.

Future Directions

Unfortunately, few people admitted to the hospital with infections are screened for OUD. Of those, even fewer are offered MOUD either for management of cravings and withdrawal or for initiation of long-term treatment. Without coordinated care of both disorders, treatment is incomplete. A call for improved integration of ID and OUD treatment has been proposed. Recently, methods were reported for an ongoing multisite randomized trial of hospitalized patients with OUD and infection comparing usual treatment (use of buprenorphine for withdrawal management with referral to outpatient MOUD) with a novel approach whereby OUD and infection treatment are managed concurrently by ID specialists and/or hospitalists. Using this novel approach, the ID specialists and hospitalists use long-acting injectable buprenorphine after a 2-day administration of sublingual buprenorphine, followed by transition to outpatient MOUD where patients may receive ID and MOUD follow-up at the same visit (158). Though outcome data are not yet available, this study identifies important considerations for hospital teams, including bundling of treatment and use of a long-acting injectable, which theoretically may eliminate some barriers to initiation of buprenorphine in the hospital and coordination of outpatient MOUD follow-up.

2. The Pregnant Patient

Pregnant patients with OUD face unique challenges and heightened stigma. This stigma is operationalized with punitive practices under the guise of “protecting” the fetus from opioid exposure. Many states have statutes that consider illicit substance use during pregnancy to be reportable as child abuse or neglect, and a few states cite OUD during pregnancy as grounds for civil commitment (159). Unfortunately, the fear of legal consequences has not been a motivator for pregnant women to cease use of illicit drugs; rather, it is a barrier that may drive women from seeking or continuing care, leading to increased risk of adverse outcomes for the mother-infant dyad (13, 160). Counseling about use of illegal substances while pregnant as well as on legal and social consequences and county, state, and local laws on medications for OUD is essential. Health care providers must know the laws in their region regarding custody of newborn or other children of mothers with untreated OUD (159, 161, 162). Many of these punitive practices play out within the construct of “deserving vs. undeserving” motherhood. Pregnant women with OUD face overwhelming shame that is often reinforced by the health care system itself and health care providers who don’t want to offer care. This may result in reduced pre- and post-natal care, or care only at delivery. In 2018, ACOG and SAMHSA published a joint clinical guide for health care providers who treat pregnant women with OUD (13). The guide is an outstanding comprehensive resource on prenatal care, infant care, and maternal postnatal care.

Approach to Methadone, Buprenorphine, and Naltrexone in Pregnancy

Clinical guidance from ACOG and SAMHSA does not recommend medically supervised withdrawal during pregnancy, as it is associated with a high rate of return to substance use, which puts both the pregnant

woman and fetus at risk (13). Pregnant women should be offered treatment with methadone or buprenorphine (13). Methadone and buprenorphine can reduce the risk of injecting drugs, which may reduce infection risk (13). These medications may also reduce cravings and withdrawal, allowing the pregnant woman to direct focus on prenatal care and stabilizing the environment (13). There is no known risk of birth defects with methadone or buprenorphine (14, 163). Historically, pregnant women being treated with combined buprenorphine/naloxone were transitioned to the single agent buprenorphine without naloxone to protect the fetus from exposure to naloxone and to avoid precipitated withdrawal if the combination drug were to be injected. There is increasing evidence that pregnant women being treated with combination buprenorphine/naloxone may not require transition to buprenorphine alone and do not experience significantly different outcomes (164-170).

There are no standardized guidelines for initial dosing of buprenorphine or methadone in pregnancy, nor for dosing adjustments as the pregnancy progresses; each patient requires an individualized assessment. As it may take days to weeks with methadone to find a stable dose, high-risk pregnancies may require hospitalization for methadone initiation to prevent illicit drug use due to untreated withdrawal or cravings during dose titration. Methadone clearance rate increases during pregnancy, typically necessitating higher dosing, especially in the third trimester (171). Dividing the daily dose can help stabilize the methadone level (172, 173). Buprenorphine similarly may need increased dosing during the third trimester (174).

There are insufficient data to support the safety of injectable naltrexone in pregnancy. Women already taking injectable naltrexone should be offered methadone or buprenorphine if they choose to discontinue naltrexone (13). As naltrexone levels fall, there will be increased agonist activity due to loss of opioid tolerance.

Peripartum Pain Control

The pregnant woman's daily dose of buprenorphine or methadone should not be expected to provide analgesia during the peripartum period, nor should buprenorphine or methadone doses be increased to control peripartum pain (13, 175). Patients with OUD are at risk for insufficient pain relief from standard therapies and may require higher doses of nonsteroidal analgesics, acetaminophen, or short-acting opioids (176). Epidural and/or short-acting opioids including morphine sulfate, fentanyl, and hydromorphone are appropriate analgesic options during labor and delivery.

Neonatal Opioid Withdrawal Syndrome and Breastfeeding

Pregnant women with OUD should be provided with education about neonatal opioid withdrawal syndrome (NOWS). NOWS may be less severe in neonates of patients treated with buprenorphine vs. methadone. There is no evidence to suggest that lower doses of buprenorphine or methadone impact the risk, intensity, or duration of NOWS (168, 177-180). Breastfeeding is recommended for women stable on buprenorphine, buprenorphine/naloxone, and methadone (13). Buprenorphine and methadone drug levels are very low in breastmilk and the poor bioavailability of naloxone through non-intravenous routes makes risk of transfer to the neonate very low (181-184). Management of NOWS in the neonate is beyond the scope of this review; the 2018 SAMHSA/ACOG Guidelines list extensive resources for clinicians (13).

3. The Emergency Department (ED)

The ED offers a unique opportunity for intervention for patients with untreated OUD. Historically, common practice for treating patients with OUD in the ED has been referral to outpatient treatment. However, a 2015 landmark study by D'Onofrio et al. (94) demonstrated that initiation of buprenorphine

in the emergency room resulted in dramatic improvements of OUD-related outcomes. Though the evidence for initiation of buprenorphine in the ED is compelling, there are many barriers to successful implementation of such programs, including funding, lack of resources, stigma on the part of health care providers, lack of training about harm reduction and MOUD, inadequate mechanisms to link patients directly to treatment, and lack of a safe and trusting space for patients to enter the health care system. Successful implementation requires the identification of well-respected champions within the department, buy-in from executive-level leadership and front-line providers, development of easy-to-use protocols (e.g., screening, brief interventions and referral to treatment/SBIRT) and tools for initiation of MOUD built into the information technology infrastructure/electronic medical record (185). Though comprehensive discussion about the approach to MOUD in the ED is beyond the scope of this resource, it is essential for psychiatrists treating OUD in the general hospital to closely collaborate with ED and upper-level leadership as ED MOUD programs are being developed.

BARRIERS

Use of medication for MOUD with buprenorphine, methadone, and naltrexone in the hospital setting has been shown to vary from institution to institution and from state to state. These variations encompass a broad range of factors, all of which inevitably serve as barriers to the delivery and receipt of care. In this section, we will illustrate different areas that we have identified as barriers to care.

1. Education

Education about opioids and OUD should optimally occur at all levels of medical training, as well as through continuing medical education programs (186). Such repetition promotes reinforcement of critical information and provides necessary updates. In addition, learning through longitudinal relationships with patients may help to reduce stigma associated with SUDs. Many physicians are unaware of or have inadequate education in identification of patients at risk for, effective evaluation of, and management of OUDs (187). Educational requirements around SUD are opaque or nonstandardized, resulting in decreased confidence in MOUD (188), and only 7% of prescribers who interact with patients with OUD have DEA waivers (189). This deficit in training begins at the earliest phases. This section will focus on the different types of learning that take place in the different phases of medical training, especially post-graduate training in psychiatry and beyond, as well as on the varied methods of education in opioid disorders.

Historically, the SUD curricula in medical schools have focused on tobacco and alcohol use disorders. In the face of the opioid crisis, however, medical educators have struggled to correct the limitations in time and inadequacy of content allocated to SUD education. Throughout the mid-to-late 2010s, the Association of American Medical Colleges (AAMC) has argued for increased incorporation of formalized OUD training in medical school curricula (190). Such education can begin as early as the first year. Some institutions have integrated opioid overdose prevention training with naloxone as an adjunct to basic life support training (191, 192). In their scoping review of SUD education in medical schools, Muzyk and colleagues noted “the lack of published curricula on OUDs” and emphasized the need for courses that highlight screening and assessment of patients, including those who are prescribed opioids as well as those using illicitly; understanding diagnosis and treatment through the lens of the chronic disease model; and specific instruction in both harm reduction and pharmacologic management (193). They suggested that problem-based learning and role-play are effective learning strategies and emphasized the importance of faculty development in these areas to provide students with real-world skills and role models to help improve care and reduce stigma. Similarly, Ratycz and colleagues suggested the use of simulation-based education to improve education on heroin and fentanyl/synthetic opioid use and enhance the biopsychosocial skill set necessary to manage patients with addiction to these substances

(194). This includes learning safe prescribing guidelines, being able to recognize risk for misuse, and understanding system-based practice for treatment and referral.

The Accreditation Council for Graduate Medical Education (ACGME) has stated that “the need to educate physicians on the treatment of addiction, for this and the next generation, is a shared responsibility of the medical school, graduate medical education (GME), and continuing medical education communities” (195). In 2019, the ACGME’s Common Program Requirements necessitated training in pain management “if applicable for the specialty,” with evidenced-based interventions for the prevention and recognition of addiction. The 2021 ACGME-sponsored GME Stakeholders Congress on Preparing Residents and Fellows to Manage Pain and SUD (196) upgraded these recommendations, which now suggest competencies in pain management, communication (including motivational interviewing and elimination of stigmatizing language), and use of medications to treat OUD for residents/fellows in all medical/surgical specialties. The 2021 Congress also developed a set of psychiatry-specific recommendations for curricular elements and educational experiences, as outlined in Figure 2.

Figure 2. Psychiatry Recommendations for Specialty-Specific Curricular Elements and Educational Experiences from the 2021 ACGME Congress (196)

- Education on the neurological, psychological, and social aspects to pain
- Cognitive behavioral therapy for managing pain
- Understanding why chronic pain is often comorbid with psychiatric disorders
- Communicating with patients about treatment options and why management of mental health is important for pain management
- How to access and refer patients to nonmedical support systems within the local community, such as support groups
- Relationship between pain and the social determinants of health, particularly in the residents’/fellows’ community
- For those residents and fellows who want to become trained in addiction psychiatry: conducting a general pain assessment; recommend treatment options to the pain care team; conducting a risk-benefit profile regarding SUD; clinical practice in treating SUD in a variety of settings for acute and chronic pain

Even with improving informal guidance by ACGME, the current ACGME Program Requirements for Graduate Medical Education in Psychiatry (197) and the Psychiatry Milestone Project (4) remain vague, with notable variability of implementation of the requirements among residency programs. Timing,

setting, and level of supervision have all been areas of inter-program inconsistency. According to a 2017 survey sent to program directors through the American Association of Directors of Psychiatry Residency Training list-serve, identified barriers to addictions training in general psychiatry residency programs reflected limitations in resources, including the use of acute general psychiatry rather than specialty clinical settings, and a lack of appropriately trained faculty (198). Fewer than 16% of programs responding had faculty who were trained or board-certified in Addiction Psychiatry, and less than 37% had faculty trained or board-certified in Addiction Medicine. Such a limitation in addiction-trained faculty affected not only clinical supervision but also design and enactment of didactic curricula (198). One study demonstrated that only a minority of residency training programs offer office-based buprenorphine treatment due to barriers including insufficient waived faculty, competing curricular demands, and lack of ancillary counseling support (199). The updated (2021) blueprint of the American Board of Psychiatry and Neurology initial certification examination now includes questions about substance-related and addictive disorders (200).

Fellowship programs, including those in Consultation-Liaison (C-L) Psychiatry, Addiction Psychiatry, and Addiction Medicine, provide advanced training in the treatment of SUDs, albeit with variations in curriculum. The Addiction Psychiatry examination does not break down in clear percentages different types of substances of abuse and their treatment. For Addiction Medicine, however, the board exam targets 10-15% of questions toward OUD, while alcohol and tobacco use disorders are each afforded 15-20% of the examination (201, 202).

C-L psychiatrists may well be the initial point of access to treatment for individuals with SUD, including OUD, whose drug use and/or complications from drug use (including the association between substance use and nonadherence with general medical care) result in inpatient medical hospitalization. C-L psychiatrists frequently are called to help with the management of withdrawal and to provide referrals for both inpatient and outpatient substance use treatment. In addition, C-L psychiatrists often provide initial treatment of SUD, including MOUD. While the inpatient medical hospital is not the best environment for longer-term substance use management, as a closely monitored setting it can be an ideal location for buprenorphine induction training for fellows. Some hospitals have a subspecialized C-L group focused exclusively on the treatment of patients with SUDs.

Only a minority of psychiatrists pursue advanced study in addiction through fellowship training. Continuing medical education programs and other resources provide lifelong learning essential for the treatment of patients with SUD. For many psychiatrists, obtaining an X-waiver to prescribe outpatient buprenorphine was neither an option nor a requirement during residency training. There are multiple ways for psychiatrists to achieve X-waiver training, including online, in person, and hybrid mechanisms. The Provider Clinical Support System (PCSS) (203), funded by SAMHSA, and the APA in collaboration with the AAAP offer X-waiver training.

Beyond buprenorphine training, several online resources provide essential, high-yield information to enhance provider knowledge base on OUD. Led by the AAAP and geared toward primary care providers, PCSS was established in response to the opioid epidemic and focuses on providing educational resources for the evidence-based treatment of OUD. The PCSS curriculum includes discussion of patient selection for medication management; medically supervised withdrawal guidelines; implementation and management of antagonist-based treatment; movement between agonist and antagonist medications; management of SUD and comorbid psychiatric conditions; treatment of chronic pain; and treatment in specialized populations, including pregnant women (203).

Other valuable resources for practitioners caring for patients with OUD include the Opioid Response Network (ORN) (204) and Project ECHO (Extension for Community Healthcare Outcomes) (205). Funded by SAMHSA, the ORN is a large national coalition with consultants in all states and nine territories who provide educational resources and training on the prevention and treatment of and recovery from OUD on a community level. Project ECHO uses a hub-and-spoke model to provide tele-mentoring in specialty areas, including the treatment of OUD, to rural primary care clinicians.

2. Institutional Policies

Current federal policy requires a DEA waiver to prescribe buprenorphine, which serves as a deterrent for many providers (206). In addition, current federal policy limits most buprenorphine prescribers, with few exceptions, to initial treatment of only 30 patients. A recent change to the U.S. Health and Human Services Buprenorphine Practice Guidelines (effective April 2021) exempts eligible practitioners from completing the previously required special training and from the requirement for concurrent provision of psychological services (207). This exemption only applies to practitioners who intend to treat up to 30 patients. Practitioners who intend to treat up to 100 patients in the first year must either be board certified in addiction medicine/addiction psychiatry or provide treatment in a “qualified practice setting.” Practitioners must still submit an NOI and obtain a waiver prior to prescribing buprenorphine (207).

From a prescriber perspective, institutional and financial barriers include the lack of adequate reimbursement of MOUD by Medicare and Medicaid (206, 208), lack of physical space and time to allow for regular follow-ups with OUD patients (188), and lack of trained support staff and specialized case managers (206). Little federal and state policy exists on the requirement for follow-up MOUD care; a recent study from Massachusetts showed in the year following overdose only 6-17% of patients received such care (209). In addition, almost two-thirds of SUD treatment facilities do not offer MOUD, and only 6% of those facilities that do offer MOUD utilize all three MOUD treatments: buprenorphine, methadone, and naltrexone (210).

3. Marginalized and Vulnerable Populations

Significant racial disparities exist in MOUD. A study of data from the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey found that of 13.4 million visits where buprenorphine was prescribed from 2012 to 2015, Black patients were on average 4 times less likely to receive buprenorphine than White patients (211). In another study of pregnant women, Black and Latinx women were less likely to receive MOUD compared to White women (212). Even following a visit to the ED for overdose, Black and Latinx patients were less likely to obtain MOUD follow-up (213). Recently, a demographic shift has been observed in the opioid epidemic, with dramatic increases in opioid misuse and overdose deaths among Latinx, African American, and Alaska Native/American Indian (ANAI) populations (214).

The Latinx population is one of the fastest-growing minority groups (expected to comprise nearly 30% of the U.S. population by 2060), and their opioid misuse rate is similar to the national population rate of 4% (215). Thus, it is essential to understand the unique sociocultural factors that influence drug use and access to prevention, treatment, and recovery in this population. Challenges that Latinx communities face include navigation of bicultural and multicultural identities, facing intergenerational and intercultural differences within households, coping with language barriers, and managing trauma and stress related to discrimination and migration. Barriers to access for MOUD for Latinx populations may include language barriers, stigma around OUD as a “moral failing” rather than a disease, fear of seeking treatment, lack of culturally responsive prevention and treatment, and less access to MAT as compared

to White people. Evidence-based prevention and treatment practices in tandem with culturally driven outreach can help address the opioid crisis in Latinx populations.

Opioid deaths, in particular heroin overdoses, have nearly doubled among Black Americans since 2000 (216). Black Americans are less likely than White Americans to be identified for substance use treatment, but more likely to be criminalized for their substance use, and Black Americans are being underserved in the current opioid crisis. Specific, targeted, and evidence-based interventions (e.g., racial impact assessments) must be provided for Black communities to counter against barriers to accessing substance use treatment and diminish the impact of the opioid epidemic.

In the U.S., ANAI people are second only to White people in the rate of overdose mortality (15.7/100,000 vs 19.4/100,000 deaths, respectively) (217), and overdose mortality among ANAI people has risen continuously from 1999 to 2016 (218). One study found evidence of racial misclassification (of ANAI race) underestimating drug overdose mortality rates among ANAI people by approximately 40% (219). Lillie et al. (220) found that younger patients and those with co-occurring substance use remain at substantially higher risk of discontinuing buprenorphine/naloxone treatment for OUD and recommended that treatment programs serving ANAI people consider paying special attention to patients with these characteristics to prevent discontinuation of treatment.

The LGBTQIA+ community has not been spared from the opioid epidemic in the U.S. (221). There is evidence that discrimination, marginalization, and victimization create elevated levels of stress (frequently conceptualized as minority stress) that can disrupt an individual's ability to regulate emotions and adaptively cope. These factors may lead to higher prevalence of substance misuse and SUDs among LGBTQIA+ populations. While MOUD is critical to address opioid use disorder among LGBTQIA+ populations, interventions addressing the specific needs of this population will play an important role in reducing treatment and access disparities. Programs that integrate behavioral health with primary care, use a trauma-informed approach, and apply minority stress principles to evidence-informed interventions (e.g., Cognitive Behavioral Therapy) have high potential for effectiveness.

The consequences of opioid misuse among older adults are significant and include increased risk of overdose, falls, cognitive and psychomotor impairments, and drug interactions (222). MOUD is underutilized in the older adult population. In a recent study, only 7.9-9.8% of total substance use-related admissions of older adults reported MOUD as part of their treatment plan (223). Challenges in this population include stigma, lack of insurance coverage, low perceived need, limited access to MOUD, and lack of patient and provider knowledge of MOUD. Buprenorphine could be a particularly useful agent for treating OUD in older adults, as it is safer in overdose and has fewer withdrawal symptoms than methadone and, unlike methadone, does not considerably prolong QTc interval (222).

Adolescent and young adult rates of opioid misuse, overdose, and death have increased steadily in the past 15 years (224). Their development, highly related to brain reward pathways, renders adolescents and young adults vulnerable to high-risk and substance-seeking behaviors. The literature guiding transitional youth (i.e., ages 16-25) MOUD is limited, and more research should evaluate the effectiveness of options other than buprenorphine, optimal treatment duration, and the benefit of adjunctive behavioral interventions in this population (225). There is a paucity of data on OUD in younger children. The CDC does not include children in its opioid prescribing guideline, citing limited evidence and lack of scope (226). The American Academy of Pediatrics Committee on Substance Use and Prevention recommends that pediatricians become familiar with screening, brief intervention, and referral to treatment (227).

Significant disparities also exist with gender. Women are less likely to receive MAT follow-up compared to men following emergency visits for overdose (213). During pregnancy, only 50% of all women with OUD receive MOUD of any form (228). This is especially devastating as women are most vulnerable to dropping out of treatment and relapsing in the post-partum period (228). See section The Pregnant Patient for more details.

Immigration status is a social determinant of health that impacts health-seeking behaviors and access to SUD treatment. According to a SAMHSA 2020 report, many undocumented Latinx immigrants do not seek MOUD for themselves or loved ones due to fear of deportation. Additionally, minorities, regardless of their immigration status, tend to view mental health and substance use treatment with suspicion, and outreach must be tailored in the context that minorities can appropriately internalize (229). Specific barriers include fear of deportation, inability to obtain identification or insurance necessary to obtain buprenorphine or methadone, denial of pending permanent residence or naturalization due to charges for drug use, and language barriers, among others (230-232). Refugees are particularly vulnerable to substance use disorders due to displacement, trauma, and stigma (233). Innovations such as digital health interventions can reduce barriers to SUD treatment for immigrants and refugees by adding privacy, reducing shame associated with asking for help, increasing access, and using adaptations to account for culture and language (233).

From a geographic perspective, rural America presents unique challenges in MOUD delivery. One-third of rural regions do not have access to any buprenorphine prescribers (234). Rural patients also face significant difficulties with transportation, with a Vermont study showing more than one in five patients missing at least one MOUD appointment due to lack of transportation (235). Despite recent improvements in insurance coverage via the Mental Health Parity and Addiction Equity Act, the act itself does not mandate insurance plans to cover mental health or substance use treatments. Indeed, 14% of Medicare and Medicaid plans do not cover any form of such treatment (212). In a 2018 SAMHSA survey, 30% of patients did not seek substance use treatment such as MOUD due to lack of insurance coverage. Even among those who qualified for substance use treatment, 20% did not know where to go or were unable to find the type of treatment they desired, illustrating a lack of outreach to these vulnerable patients (236). In a review of clinical records at a local Veterans Affairs hospital, veterans with housing assistance and case management have been shown to be 4.5 times more likely to engage with MOUD programs (237).

The literature overwhelmingly demonstrates perceived stigma by patients as a barrier to engage with MOUD. Frequently, patients defer MOUD because they feel they are replacing one addiction with another (188). Similarly, some patients and their families believe that MOUD should be the last-line rather than first-line treatment for substance use (189). Health care providers may also contribute to this stigma, as seen in cohorts of clinicians who believe in a solely abstinence-based approach to SUD treatment (189).

4. COVID-19 Pandemic

By fueling the next wave of the opioid crisis, the COVID-19 pandemic has been a barrier to the management of OUD (238). Drug overdose deaths in the United States previously set a record high in 2019 per the CDC (70,980 projected overdose deaths, with over 50% of these deaths involving fentanyl and other synthetic opioids) (239). Unfortunately, the final 2020 total in the United States could exceed 90,000 overdose deaths, which would represent the largest single-year percentage increase in the past 20 years (240). Individuals with OUD become more vulnerable during a pandemic, as they are often

alienated from traditional news sources and less likely to learn about their risk of infection and best practices (238). During the pandemic, they are more likely to use opioids alone (where another person is not around to administer naloxone to reverse the overdose) due to social distancing and lockdown measures (241). They frequently suffer from financial insecurity, live in shelters or prison, have medical comorbidities and reduced access to health care, or are less able to follow pandemic-related guidelines. Moreover, individuals with OUD can be skeptical of authority (e.g., due to previous interactions with law enforcement). Drugs are harder to obtain in this climate, and people may substitute drugs with substances with which they are less familiar, thereby increasing risks of adverse effects (238). Thus, disruption of drug supply chains can paradoxically cause overdoses to increase as supplies go down. There is also less access to treatment programs, in particular residential rehabilitation centers and in-person groups. Video sessions are difficult to attend for homeless individuals or those without a cell phone. Telepsychiatry appointments also may make it more challenging for clinicians to detect intoxication (e.g., it may be harder to see pupil constriction from opioid intoxication).

On a more positive note, the easing of restrictions by SAMHSA and the DEA to decrease COVID-19 infection risk and spread has allowed health care providers unprecedented freedom to prescribe medications for OUD treatment via telemedicine (e.g., take-home 28-day doses of methadone, new buprenorphine prescriptions after an initial telephone call) (242). The DEA leveraged the public health emergency exception to the Ryan Haight Online Pharmacy Consumer Protection Act, which restricts the prescribing of controlled substances via telehealth with certain exceptions, and this has helped improve access (243). Several states currently have reciprocity so that physicians do not have to obtain licensure in other states to treat patients there (though this is unlikely to be permanent). The continued easing of these restrictions and limitations could increase access and ability to meet patients “where they are at.” Many hope that these streamlined changes can become the “new normal” as the pandemic subsides.

CULTURE CHANGE THROUGH DAY-TO-DAY LIAISON WORK

1. Easing Teams Through Stigma

Overview of Negative Impact of Stigma and Patient Outcomes

The presence of stigma against mental health patients is pervasive and can lead to a lower quality of medical care across multiple medical subspecialties (244). Stigma severity increases as perceived cause and control over a condition increase, with a high perception of such regarding SUD patients (245). There are three frameworks for considering stigma in mental health care: structural, interpersonal, and intrapersonal stigma (244). Identifying and understanding these frameworks may provide opportunities to remove barriers to higher-quality care. Structural stigma occurs at the institutional level and encompasses societal values, cultural norms, and organizational policies that shape inequality of power and resource allocation (246). These can reflect the beliefs that people with addiction may be less treatable and less deserving of care. At the interpersonal level, non-stigmatized groups can harbor negative beliefs about stigmatized groups. Intrapersonal or self-stigma can be internalized as a sense of shame, leading to further sense of alienation and disempowerment. In its most extreme form, self-stigma can lead a patient to believe that perceptions of self are true, e.g., they are worthless, undeserving, or a failure, which ultimately results in disengagement from care.

Diagnostic overshadowing, which refers to a misattribution of physical symptoms to preexisting mental illness, can lead to reluctance to initiate investigations of underlying disease based on symptoms (247). For example, if a patient presents with physical symptoms in the setting of known history of depressive disorder, there may be a resistance to perform further investigation to determine an underlying cause of

the presenting symptoms. This phenomenon, coupled with the burden of stigma, may lead to further isolation by the patient or avoidance by the provider, which can ultimately delay treatment.

Several strategies have been proposed on how to combat or minimize mental health stigma, including the increase of education in addiction biology. Specifically, regarding patients on MOUD, understanding the neurobiological mechanisms of addiction in addition to the psychosocial contributors can help decrease stigma. During the progression of SUD, evolutionary neurobiological adaptations are underway as the individual progressively loses control over goal-directed behaviors and their ability to adapt their response to drug-reward stimuli (248). Increasingly, through disease progression, individuals develop dysphoric states requiring more alleviation of distress by means of biologic reward, such as opioids. Understanding how underlying biological changes lead to changes in behaviors in addiction could help shift blame from the individual and mitigate the widespread belief that opioid-seeking behaviors are solely under the individual's volition. This biologically based education can be used for all health care providers taking care of patients with OUD (Figure 2 and Supplement Handout).

Highlight Success Stories: Case conferences highlighting patient success stories and “where are they now?”

In academic hospital settings, subspecialists routinely gather for morbidity and mortality (M&M) case conferences that aim to create a nonjudgmental space where errors can be reframed to identify system-based problems or highlight patient safety issues. Due to already high rates of perceived inability to help patients with OUD, an alternative to the M&M conference may include case presentations highlighting OUD patient success stories. Involving individuals with lived experiences of prior substance use to develop a partnership with the treatment team can be an effective measure of bridging the gap between populations.

Recruiting Champions and Empowering the Front Line to Improve Buy-in: Providing education on harm reduction

Adapting harm reduction in the hospital setting is a way to reduce negative consequences of substance use. Multiple barriers include continued use of stigmatizing language, low ease of identification and consulting addiction services, lack of resources for safe use, and low staff education and access to appropriate treatments and aftercare (249). Harm reduction begins with empowering staff with knowledge regarding SUD and instilling the belief that it is a treatable disease. This begins with changing the language used when discussing patients with OUD or speaking with patients directly.

Figure 2. Talking to Health Care Providers About Opioid Use Disorder and the Brain

OPIOIDS, the REWARD PATHWAY, and the BRAIN

Opioid use disorder is a condition where the brain becomes hijacked by its own reward pathway. After exposure to opioids, the reward pathway drives a person's decisions and actions to get more opioids. It steers the person like a car with the gas pedal floored and the brakes cut.



The Gas

The **Ventral Tegmental Area (V)** scans the environment and releases DA (presses the gas pedal) when it senses a pleasurable stimulus, like opioids. The **Nucleus Accumbens (NA)** senses the DA and releases more DA.

The Steering Wheel

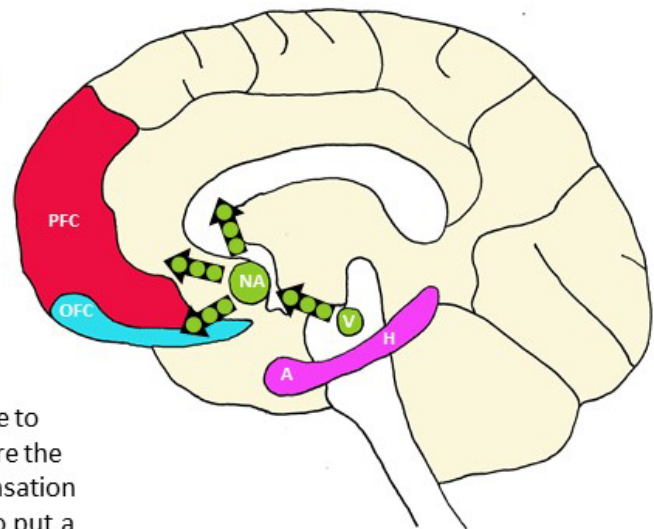
The **Orbital Frontal Cortex (OFC)** senses DA and "steers" the person toward the pleasurable stimulus. The more DA, the more difficult it is to steer in a different direction.

The Driver's Emotional Memory

The **Amygdala (A)** and **Hippocampus (H)** work together to remember stimuli that produced positive emotional experiences. They remind and reinforce to the VTA and NA that opioids should be sought after.

The Brake

The **Pre-Frontal Cortex (PFC)** acts as a brake to override the gas and steering wheel. The more the brain has been exposed to the pleasurable sensation of opioids, the more difficult it is for the PFC to put a brake on other parts of the reward system.



● = Dopamine (DA)

Talking to Healthcare Providers about Opioid Use Disorder and the Brain©
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Perceptions by patients regarding language have the potential to affect patient-internalized stigma and prognosis (245). A primary example of nonstigmatizing language in referring to a patient as someone “having substance use disorder” in contrast to referring to them as “a substance abuser,” or having a “urine test positive for opioid,” versus “a dirty urine.” Language has a potentially large impact on the attitude of community perception as well, in turn affecting policy change. When discussing implementation of safe sites for patients to access clean supplies for opioid use, nearly half of participants said they supported the legalization of “overdose prevention sites,” compared to only 29% in support of legalization of “safe consumption sites” (250). Lists of alternative terms (Table 4) can be distributed to personnel.

2. Make Treatment Easier for Providers (IT infrastructure, MOUD-specific protocols/tools built into EMR, bridge clinics)

Delays or deficits in care are in the products of unfamiliarity in treating OUD in the hospital. The impact of automated order sets on physician behavior has been studied in many settings, and overall improvements in clinical outcomes have been shown (251-253). No studies have explored the utility of automated order sets to treat opioid withdrawal while a patient is in the hospital. However, some hospitals have begun to include buprenorphine order sets along with COWS instructions in physician order entry. This may reduce barriers to ordering MOUD, in turn improving access and clinical experience.

Table 4. Examples of Person-First Nonstigmatizing Language [Adapted from NIH National Institute on Drug Abuse]

Avoid	Say	Rationale
Addict	Person with substance use disorder	Shows that the person “has” a problem rather than “is” a problem
Substance/Drug abuser	Patient with [opioid] addiction	Avoids individual blame
User/Junkie	Patient	Avoids moral judgement
Former/Reformed addict	Person in recovery	Restores empowerment
	Person who previously used drugs	
Habit	Substance use disorder, addiction	Removes implication that person is “choosing” to use substances or can choose to stop
Abuse [Illicit]	Use	Removes negative judgement and punishment
Abuse [Prescription]	Misuse/Use other than prescribed	
Opioid replacement therapy	Medication treatment for OUD	It is a misconception that medications “replace” or “substitute” one drug/addiction for another
	Opioid agonist therapy	
	Pharmacotherapy	Removes stigma that patient is not sober
Clean [toxicology]	Testing negative	More clinically accurate and in alignment with descriptions of other medical conditions
Clean [individual]	Person in remission/recovery	
	Not in active use	
Dirty [toxicology]	Testing positive	Improves patient’s sense of hope and self-efficacy of change
Dirty [individual]	Person with active substance use	
Addicted baby	Baby born to mother who used [opioids] while pregnant	

	Baby with signs of withdrawal from prenatal drug exposure	Babies cannot be born with addiction since addiction is a behavioral disorder; they are born manifesting a withdrawal syndrome
	Baby with neonatal opioid withdrawal syndrome	Prioritize clinically accurate diagnoses, same as for other medical conditions
	Newborn exposed to substances	

3. Acknowledging Punitive Policies and Their Carceral Association

Structural stigma is apparent in several areas related to the criminal justice system; many institutional policies treat SUDs as a criminal issue rather than a health concern. Several aspects of care can be perceived as punitive to the patient, notably the need for repeat urine tests, a safety sitter, or 1:1 security presence. Protocols that are institutional level can promote further self-stigma at several points through the course of hospital admission. This begins at time of admission, when patients may have to change into hospital garb under observation due to contraband concerns. Patients may also be denied access to belongings or be subject to wellness checks of their room or personal effects. Patients may have home doses of methadone or buprenorphine/naloxone held until the dose can be confirmed by an outside MOUD provider. Stigma can be further amplified at time of discharge planning when patients may be denied admission to the next level of care due to active MOUD prescription. An examination of carceral associations and triggers within existing hospital policies would be beneficial, given the potential of such policies to result in distrust and further deterioration of the physician-patient relationship.

4. Education of Trauma-Informed Care

Co-occurring post-traumatic stress disorder (PTSD) and prior trauma are highly prevalent in patients with OUD and can impact clinical outcomes as well as the patient-provider relationship (254). Data from the Adverse Child Experience study revealed dose response associations between number of adverse experiences and worse mental and medical health outcomes, including increased risks of substance use in adulthood (255). Following trauma, the stress response triggers a cascade of neurotransmitters and hormones that can serve as short-term protective mechanisms. With prolonged elevations, however, these stress responses can negatively influence lifelong neurodevelopment and behavior, resulting in a hypervigilant state where anxiety and fear can easily manifest following respective triggers (256, 257). Given the unpredictable nature of the stress response, it can be difficult to predict what environmental factors may cause an increased trauma response, and therefore the application of universally based trauma informed care is recommended to maximally encompass clinical scenarios (258).

Common instances where there can be high likelihood of causing a trauma response include physical or pelvic examination, preparation for endoscopy procedures or imaging exams, or preventing a patient from leaving a small room. In some instances, the patient would have to lie in a specific position or maintain a vulnerable position, for example having limbs externally rotated, mouth open, or back toward the examiner, for prolonged periods. One potential strategy is knocking and announcing your entrance into the room. Another could be thoroughly explaining the steps of an upcoming procedure or physical exam prior to starting the exam, including details such as expected duration or location of physical touch on patient (259).

Several key elements have been identified in the practice of trauma-informed care, including the notion that trauma influences interpersonal relationships and experiences of treatment, the importance of recognition of trauma histories, the respect for privacy as well as physical and emotional safety, and the

avoidance of triggers from past trauma. Through these tenets, the goals of trauma-informed care extend beyond the avoidance of triggers and include promoting patient-centered care and promoting an individual's strengths while supporting their resilience and self-efficacy (256).

5. Understanding the Impact of Patient-Centered Discharges

Data show significantly worse outcomes and increased risk of mortality with readmission of patients previously discharged AMA (260). Identifying risk factors for a patient seeking discharge AMA may help reduce future occurrences, and there have been several predictors consistently identified in patients who have greater tendency to be discharged AMA. Notably, these include younger age, male sex, lack of insurance, history of substance use or mental health illness, lack of a primary care physician, living alone, and prior hospitalizations (261). Additional factors include undertreated pain or withdrawal symptoms, co-occurring nicotine withdrawal, social obligations at home, and comorbid PTSD and triggered anxiety because of hospitalization. Methadone use while in the hospital was a protection against AMA (117), further promoting the idea that well-managed opioid withdrawal symptoms can allow for improved patient experience, in turn allowing for completion of medical care. One study found that the largest diagnostic category associated with discharge AMA was having a mental health disorder, with African Americans proportionally having the highest risk (262). This highlights the impact of structural stigma as it pertains to mental health and racism and highlights the need for further improvements in health care delivery across all patient populations. Another review points out that AMA behavior may be more related to a combination of factors of admission and hospitalization than to a breakdown in the therapeutic alliance between physician and patient (263). The authors further promote the utility of being able to recognize psychological factors that precede AMA behavior and the benefit of motivational interviewing as a primary nonjudgmental tool to help understand how patients make decisions to self-discharge.

6. Shared Decision-Making

Reflective of the nature of OUD and its multidimensional aspects, treatment decision-making is best when shared between the multiple members of the treatment team and patient. Commonly, the hospitalized patient with OUD faces numerous complex decisions, including where to proceed with the next level of care and choice of MOUD, in addition to whether to seek further treatment of mental health and medical conditions post-hospitalization.

Multidisciplinary meetings are becoming increasingly prevalent for hospitalized patients. Use of a substance use intervention team has been found to decrease hospital length of stay and promote regular discharge to the home (264). Specifically, the psychiatrist on the team can serve as an addiction educator, bringing knowledge of the basis of neurobiology of addiction and how the patient subsequently relates to the world. The psychiatrist can also help manage co-occurring mental health conditions, thus optimizing patient care.

Another study has promoted the idea of increased collaboration within health care teams by demonstrating a measurable increase in initiation of OUD in patients admitted for endocarditis who participated in the multidisciplinary approach (265). This model not only brought multiple specialties to the table but included education of caregivers at home. Moving forward, involvement and contribution of the primary team, trained support staff, family, and patient will be key in the success of treatment of this severe relapsing and remitting disease, thanks to the augmentation of the expertise of each respective specialty.

CONCLUSIONS

It is essential that health care systems actively engage patients with OUD who are being treated in the general hospital. Psychiatry must own its role as expert in the treatment of SUD by acknowledging and combatting residual stigma within the field. Furthermore, education leaders at all levels of medical training, from medical school through graduate medical education, must actively address the dearth of opportunities to receive adequate experience in the treatment of addictions. Psychiatrists working in the general hospital setting should practice evidence-based care of patients with OUD, including the use of MOUD. Psychiatrists must also play a role in reducing stigma. It is imperative that psychiatrists who identify a personal education gap take action to remedy this deficit through continuing medical education. Likewise, health care systems, accrediting bodies, and relevant medical boards should incentivize OUD treatment education and training for all health care providers involved in the care of patients with OUD.

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