Journal of the Academy of Consultation-Liaison Psychiatry 2025:■:■–■

C-L Case Conference

C-L Case Conference: Challenges of Managing Severe Opioid Use Disorder in the Hospital

Kahlo Baniadam, M.D., Brent D. Schnipke, M.D., James L. Levenson, M.D., Megan Buresh, M.D., Rachna S. Raisinghani, M.D., Elizabeth Ryznar, M.D.

Consultation-liaison psychiatrists are frequently consulted to assess and manage severe opioid use disorder in hospitalized patients requiring treatment for complications related to their opioid use disorder. We describe the case of a 43-year-old male with severe opioid use disorder who recently underwent bilateral amputations for his leg wounds at another hospital and left before medically advised. He subsequently presented to our hospital for pain and was admitted for ongoing infection. An understanding of the ethical considerations surrounding patient-directed discharge (previously referred to as "against medical advice"), appropriate opioid agonist dosing strategies, and post-discharge planning can improve outcomes for these patients, who often face significant stigma within the health care system.

(Journal of the Academy of Consultation-Liaison Psychiatry 2025; ■:■–■)

CASE DESCRIPTION

A 43-year-old male with severe opioid use disorder (OUD), complicated by ongoing intravenous drug use, hepatitis C, and chronic leg wounds status postrecent bilateral above-the-knee amputation, was admitted for suspected wound infection and severe bilateral lower extremity pain.

Ten days before this admission, the patient was admitted to one hospital for sepsis secondary to deep leg abscesses; amputation was planned. He used illicit substances there and requested to leave before completion of medical treatment due to inadequate pain control. The discharge summary documented that he had capacity to leave "against medical advice" (AMA). Notably, he was in the intensive care unit receiving a norepinephrine drip at the time of discharge, indicating some cardiovascular instability that placed him at higher risk of complications from premature discharge. Several hours later, he presented to a second hospital for pain and was admitted for sepsis. He underwent bilateral above-the-knee amputation, with his hospital course complicated by in-hospital injection of illicit opioids, difficult-to-control pain despite administration of fentanyl and ketamine patient-controlled analgesia pumps, and verbal agitation. After initial refusal, he agreed to start methadone at 40mg, with plan to titrate by 10mg each day. The next day, after receiving 50mg of methadone and undergoing a needed revision surgery, he became agitated again and requested to leave. The surgical team determined he had capacity to leave "AMA" and discharged him.

The following day, he presented to our institution's emergency department for severe pain and was admitted for sepsis. He reported using heroin after leaving the second hospital and had not picked up his antibiotic prescription. Psychiatry was consulted on hospital day 2 to manage his OUD. History revealed

Received March 11, 2025; revised June 12, 2025; accepted June 17, 2025.
From the Department of Psychiatry (K.B.), University of Maryland Medical Center, Baltimore, MD; Department of Psychiatry and Behavioral Sciences (B.D.S.), Northwestern University Feinberg School of Medicine, Chicago, IL; Department of Psychiatry (J.L.L.), Virginia Commonwealth University School of Medicine, Richmond, VA; Division of Addiction Medicine (M.B.), Johns Hopkins University School of Medicine, Baltimore, MD; Division of Consultation Liaison Psychiatry (R.S.R., E.R.), Sheppard Pratt Health System, Baltimore, MD. Send correspondence and reprint requests to Kahlo Baniadam, M.D., 701 W Pratt St, Baltimore, MD 21201; e-mail: Kahlo.Baniadam@gmail.com

that he started taking prescription opioids in his early 30s for back pain and then progressed to intranasal and injection opioid use for 8–9 years. For the past 2 years, he reported injecting 4–10 capsules of 1-gram fentanyl/xylazine mixture daily, which led to chronic leg wounds. He had previously tried both buprenorphine-naloxone and methadone to help with cessation. He achieved 6 months of sobriety several years ago.

He expressed goals of regaining sobriety, learning how to walk again after the bilateral amputation, and acquiring better housing. On exam, he appeared comfortable and had 2-3mm pupils. His thought process was organized. As the interview progressed, he became more irritable and requested to stop. There was no evidence of depression, mania, psychosis, or cognitive impairment. We recommended resuming methadone at 40mg with an increase to 50mg the following day. We transferred him to the locked medical unit in our hospital with a belonging search, given recent use of illicit substances during his prior hospitalizations, as per our hospital policy.

On hospital day 3, his hemoglobin dropped from 8.2 g/dL to 6.8 g/dL. He refused blood draws and blood transfusion, as well as wound care for his postsurgical site. He requested to leave the hospital and psychiatry was asked to evaluate capacity for premature discharge. On our evaluation, he reported he had untreated pain and disliked the locked unit. He understood that he had an infection, agreed to take an oral medication, and promised to return to the hospital if his condition worsened. He did not express understanding of a possible unidentified source of bleeding. In contrast with earlier examination, he now appeared uncomfortable with significant irritability and dilated pupils (6mm) despite recently receiving 4mg oral hydromorphone (16 Morphine Milligram Equivalents [MMEs]). We determined that he lacked capacity for self-directed discharge *in that moment* because his pain and withdrawal symptoms impacted his ability to appreciate and reason about the risks and benefits of remaining hospitalized in light of his infection, bleeding risk, and recent surgery; furthermore, his choice ran counter to his previously expressed goals in the absence of withdrawal.

We spoke frankly with him about our assessment. Importantly, we acknowledged that his severe withdrawal symptoms and pain were causing his discomfort and reassured him that we wanted to work with him, not against him, to reach his goals of sobriety, rehabilitation, and housing. We asked him to give us an opportunity to treat his pain and withdrawal immediately, and he agreed. We ordered 1.5mg intravenous hydromorphone (30 MMEs) immediately. We told him we would return in 30 minutes to reassess him. He agreed to not to leave in that time. Upon our return, he still had objective signs of withdrawal, so we ordered another 1.5mg intravenous hydromorphone (30 MMEs), which required justification to the pharmacist and nursing staff given that he had already received 50mg of methadone and 46 MMEs that day. After the second dose of intravenous hydromorphone, his pupil size normalized, his mood relaxed, and he appeared more comfortable. We acknowledged that we had under-dosed him earlier and reiterated our desire to partner with him to achieve his health goals. We explained that we will treat his withdrawal and pain aggressively over the next few days, whereas cautioning that he may occasionally experience some short-term discomfort while we found the right dosing strategy. The patient consented to continued hospitalization and agreed to nursing interventions and blood transfusions for his other medical issues.

Subsequently, we increased his methadone by 10mg every 1–2 days and used additional agonists (hydromorphone patient-controlled analgesia and as needed oral oxycodone or intravenous hydromorphone) to manage breakthrough symptoms. He eventually stabilized on methadone 80mg with as needed acetaminophen and oxycodone for breakthrough postsurgical pain. We had communicated to the primary team that if he were to ask for patient-directed discharge again, then he should be assessed for withdrawal and pain and treated accordingly. However, he never requested patient-directed discharge after that initial episode and he continued to consent to hospital care interventions. Toward the end of his hospitalization, he spontaneously expressed gratitude for not being immediately discharged during the initial episode, acknowledging that his desire to leave was "the drugs talking."

The service encountered several hurdles when referring him to subacute rehabilitation (SAR) for preprosthetic training. Few facilities allowed patients to take methadone, and those that did required prior enrollment in a methadone clinic. Eventually, a clinic was located that conducted telehealth intakes and could deliver methadone to the SAR. Given a possible delay in shipping, the accepting SAR requested a 3-day bridge of methadone. Our hospital pharmacy initially

refused, stating that outpatient methadone could not be dispensed for use after hospital discharge for a substance use disorder diagnosis. After clarifying the Federal Drug Enforcement Agency rules, the pharmacy dispensed the methadone, and the patient was discharged to SAR.

OPIOID AGONIST DOSING STRATEGIES (DR. BRENT SCHNIPKE)

Hospital-based management of severe OUD can present many challenges. OUD is among the most common substance use disorders encountered in hospitalized patients, and chronic dependence on opioids can have significant effects on other health conditions; despite this, it remains underrecognized.[1] Even when recognized, sufficient treatment of opioid withdrawal symptoms is uncommon. One option includes using short-acting opioids to effectively treat pain.[2,3] Less than 30% of patients with OUD are offered medications for opioid use disorder (MOUD) across all settings.[4] In hospitalized patients, there are additional complicating factors, like comorbid pain, interactions with other medications (such as sedatives, anxiolytics, or anesthesia), restrictive environmental factors (such as policies prohibiting use), and the overlap of withdrawal symptoms with other conditions; these factors can contribute to discharges AMA.[5]

In recent years, most illicitly obtained opioids are partly or wholly contaminated with fentanyl or other high potency synthetic opioids (HPSOs). Additional contaminants (such as xylazine in this case) are also common and can have compounding effects on both intoxication and withdrawal states. The intoxication, chronic dependence, and withdrawal states from HPSOs are more potent and intense than naturally derived opioids (such as heroin and morphine). Because of this, doses needed to manage withdrawal symptoms, or even comorbid pain, are often higher in the modern era than was common before the widespread use of HPSOs.

Chronic opioid use is well-known to lead to tolerance, meaning that pain is often undertreated for patients with OUD. Cross-tolerance between different opioid formulations is incomplete but generally accepted to be substantial.[6] MMEs are helpful for estimating the dosage of an opioid medication that may correspond to quantity of use but can be inaccurate as the exact components of illicit opioids are frequently unknown. Thus, higher doses than expected from a simple dose conversion are frequently needed.

Opioid withdrawal is characterized by a cluster of symptoms which are extremely unpleasant and are a common reason for patient directed discharges. Recognition of withdrawal symptoms is the first step to minimizing this, but undertreatment remains common.[7] Reasons for undertreatment may include provider discomfort with specific medications or dosages, lack of education about doses needed to manage symptoms, provider concern for creating, worsening, or "rewarding" addiction, and interpersonal factors such as a patient's behavior or attitude that contribute to undertreatment.[8]

Treating opioid withdrawal with short-acting opioids is an option that has been used in hospitalized patients.[2,3] However, in the era of HPSOs, rapid induction with both MOUD agonist therapies is increasingly common and can address the issue of undertreatment and comorbid pain. Standard recommendations for methadone are to start at 40mg daily and increase slowly, due to methadone's long half-life and slow rise in blood levels. However, 40mg is likely the minimum effective dose to control withdrawal symptoms and probably is ineffective for many patients with high tolerance, such as this patient, whose reported daily use suggests a target dose of at least 100mg of methadone (based on morphine milligram equivalents). Starting at doses above 40 mg, especially when the patient is not methadone-naïve, is becoming more common[9] and this patient would have likely tolerated a higher initial dose (for example, 60 or 80mg) followed by a slower titration in subsequent days to avoid overdose. An alternative strategy, as applied in this case, is to increase quickly over a few days. A faster titration may have addressed his withdrawal symptoms more effectively: for example, starting at 40mg and increasing by 20mg each day until reaching the expected target dose. Recent case series have shown success (and limited adverse events) using even more rapid protocols that allow for 60mg on day 1 and achieving 100mg by day 3 for select patients.[10,11]

Rapid titration of buprenorphine is also possible, and its use is often preferable because of lower barriers to accessing aftercare. Its partial agonism buffers against unintentional overdose because of the ceiling effect: even very large quantities of buprenorphine will not overactivate the opioid receptors. This means that

overdose (and even euphoria) is uncommon. For patients in opioid withdrawal, single doses of 24 mg or 32 mg of buprenorphine have been used to quickly stabilize opioid withdrawal.[12,13] Tolerating enough withdrawal to complete a "standard" buprenorphine induction is simply not possible in many patients, particularly those with comorbid pain and those using large quantities of HPSOs. Other titration strategies with buprenorphine, such as a low-dose buprenorphine induction can also be done in inpatient settings. For these, the patient is given low and increasing doses of buprenorphine while continuing high doses of any full agonist of choice. Low-dose buprenorphine induction is advantageous because it does not require the patient to discontinue full agonists until they are already stabilized on buprenorphine, and if successful, it will not cause any withdrawal symptoms. Low-dose buprenorphine inductions are typically done with intravenous administration,[14–16] buccal films,[14,15] or buprenorphine patches.[17] An example is in Table 1, with additional examples in the references.[14–19]

THE ETHICS OF PATIENT-DIRECTED DISCHARGE (DR. JAMES LEVENSON)

Leaving the hospital before medically advised (previously termed "AMA discharge") occurs for many reasons, including lack of understanding of the illness or treatment, substance craving and/or withdrawal, disagreement with treatment plans, anxiety, conflicts between patients and staff, concern for the security of pets or dependents, and unstable housing. They consistently represent about 1% of hospital discharges. The term "AMA discharge" first appeared in the 1950s in reference to patients with tuberculosis who wished to leave the hospital before completing antibiotic treatment. Although hundreds of articles have been published since then, AMA has no specified legal or formal clinical meaning. No reference can be found to it on the Joint Commission site. The term refers to patients who request hospital discharge sooner than their providers think best.

TABLE 1. Low-dose Buprenorphine Induction Timeline

Day	Opioid agonist (prescribed or nonprescribed)	Buprenorphine dose
1	Full dose	150 mcg IV buprenorphine (approx. 0.5mg SL), q6hrs x4 doses
2	Full dose	300 mcg IV buprenorphine q6hrs x4 doses
3	Full dose	600 mcg IV buprenorphine q6hrs x4 doses
4	Full dose	2mg-0.5mg SL buprenorphine q6hrs x4 doses (TDD = 8mg-2mg)
5	Discontinue	8mg-2mg SL buprenorphine BID

BID = twice daily; IV = intravenous; SL = sublingual; TDD = total daily dose.

"AMA discharges" often represent a failure in shared decision-making and are inconsistent with patient-centered care.[20] From an ethical perspective, capacitated patients' right to consent to or refuse treatment is grounded in the principle of Autonomy. Physicians' obligation to advocate for the best medical outcome for the patient is the essence of the principle of Beneficence. Balancing these 2 perspectives is the basis for informed consent. When patients' wishes and physicians' treatment plans conflict, the former take precedence, except under certain legally defined exceptions, such as involuntary psychiatric treatment. The term "AMA discharge" reflects a paternalistic perspective that also stigmatizes people as bad or uncooperative. Neutral terms like "informed refusal" or "patient-requested discharge" are not yet widely used, though in the field of addiction medicine "patient-directed discharge" is gaining traction.

"AMA discharge" requests can provoke a range of defensive responses in providers. Providers and hospitals overly focus on reducing liability by asking patients to sign an AMA discharge form; however, such a form is not legally required and does not constitute informed refusal of care. What *is* clinically appropriate and will mitigate liability is documentation in the medical record that a full discussion of risks and benefits has occurred and that the patient demonstrated understanding. Providers sometimes tell patients that insurers will deny payment for premature discharge; such statements are false and coercive. Providers sometimes refuse to provide discharge medications or follow-up appointments. Such an all-or-nothing stance violates the obligation to provide the best care possible, which may entail compromise.[21] For example, if a patient declines to stay hospitalized for weeks of IV antibiotics, and oral antibiotics would be better than none, the latter should be prescribed. In some cases, self-directed discharge may prevent teams

from having time to establish follow-up care, which should be part of the informed consent to self-direct discharge.

Conflicts over inpatient opioid dosing are common and frequently trigger premature discharge. Harm reduction is a useful framework in these situations. Harm reduction refers to a range of clinical and public health practices designed to lessen the negative consequences of human behaviors and has been most commonly applied to drug use, as reflected in the provision of naloxone, sterile syringes, fentanyl test strips, and safe consumption sites. This approach stems from a consequentialist ethical perspective that considers the benefits and risks of each alternative, whereas striving to maximize benefits and minimize adverse outcomes. In contrast, insisting that minimization of drug use be the primary aim risks violating ethical principles.[22] Empirically, provision of medications for OUD (methadone or buprenorphine) on the day of admission reduces premature discharges.[23] For medically hospitalized patients who have OUD or other SUDs, access to expert and culturally competent resources is key to reducing stigma and self-directed discharge.[24] Hospital policies sometimes create barriers that prevent timely and effective opioid substitution therapy, aggravating withdrawal and increasing the risk of self-directed discharge.[25] However, even when such medications are prescribed, insufficient amounts lead to premature discharge.[26] Another potential cause of premature discharge is clinicians' underestimation of opioid dose requirements in chronic opioid users due to tolerance and hyperalgesia.[27]

In this case, within 8 days the patient was in 3 hospitals, leaving the first 2 prematurely in a medically unstable state. Methadone was provided at the second hospital several days after admission, starting at 40 mg and increasing to 50mg the subsequent day, at which point he left. The third hospital restarted him at methadone 40 mg despite evidence that this was insufficient. His reported use of fentanyl amounted to 520–1300 MME/day, whereas 40 mg of methadone equals less than 200 MME/day. His pupils indicated he was still in withdrawal even with extra opioids given. From a harm reduction standpoint, liberal methadone dosing was justified as risks from lack of cooperation with treatment and leaving hospital before medically advised seriously endangered him.

Was it ethically justified to retain the patient against his will? To what extent do acute withdrawal and pain undermine a patient's capacity for decision-making? A full discussion is beyond the scope, but it is not sufficient to note that opioid use impacts executive functioning and emotional regulation because so do other conditions (e.g. major depressive disorder) that do not automatically negate capacity. If patients' suffering (of any cause) makes them unable to engage in discussion including demonstrating understanding of risks and benefits, then they do not have the capacity to consent to/refuse treatment. In this case though a more appropriate dose of methadone from the start might have prevented AMA discharges.

DISCHARGE PLANNING BARRIERS (DR. MEGAN BURESH)

Rates of hospitalizations from medical complications of OUD have increased dramatically in the past 2 decades,[28] many of which are due to infectious complications of injection drug use.[29] Many of these patients require ongoing medical care after hospital discharge, such as IV antibiotics for 4–6 weeks and wound care. This patient required physical therapy for preprosthetic training post–above-the-knee amputation. Like this patient, more than 25% of hospitalized patients with OUD are referred to SAR, also known as skilled nursing facilities, a higher rate than for patients without OUD.[30] Part of this is due to stigma by home care agencies who refuse medically eligible patients for home IV antibiotics and wound care due to recent drug use,[31] despite evidence that it can be done safely.[32]

Unfortunately, SARs frequently discriminate against patients with substance use disorders and disproportionately reject patients with OUD.[33,34] There is an additional level of stigma against the opioid agonist MOUD, methadone and buprenorphine, with lowest likelihood of acceptance for patients receiving methadone in one study.[35] Rejection of patients due to their substance use disorder, or receipt of MOUD, is a violation of the American Disabilities Act and should be reported to the Department of Justice.[36] Patients with SUDs referred to SAR have longer length of stay, limited facility choice and subpar medical care.[37,38] During these prolonged hospitalizations, patients are at high risk of leaving the hospital by patient-directed discharge.

Some of the stigma against methadone stems from the complex federal, state and local regulations that

restrict use of methadone. Due to federal regulations unique to the United States, methadone cannot be prescribed for OUD but must be dispensed by a federally regulated opioid treatment program (OTP), or methadone clinic. Acute care hospitals are not subject to many of the regulations governing OTPs, and can initiate and dispense methadone to admitted patients, as was done appropriately in this case. Under current regulations, unlike acute care hospitals, subacute facilities cannot dispense methadone for OUD. As with this case, a patient must be enrolled in a methadone clinic before hospital discharge and arrangements must be made for provision of methadone once patient arrives at SAR. Traditionally, OTPs would either deliver or mail the methadone to the SAR after the patient arrived at the facility. This frequently led to delays in receipt of methadone, putting patients at risk of opioid withdrawal. Fortunately, recent changes to Drug Enforcement Administration regulations governing the "Three Day Rule," now allow acute care facilities to discharge a patient with 3-day supply of methadone at once, rather than one day at a time.[39] Although feasibility of dispensing methadone at hospital discharge has been successfully implemented at multiple centers,[40,41] ongoing education of hospitals and pharmacies is needed, as seen in this case.

Although these barriers are complex, this case illustrates that with effective advocacy by the hospital care team, methadone can be successfully initiated at the hospital and continued at SAR, as demonstrated in the clinical pilot, OUD MEETS in Baltimore.[42] At a systems level, better integration of addiction treatment with other medical treatment is needed to give patients more choice on where they receive care – including integration of medical care into inpatient and residential treatment facilities, expanding access to home care for people with SUDs, as well as advocating for MOUD access at SARs. One solution to integrate care is for direct linkage between SARs and OTPs. There is also discussion of expanding access to methadone in the United States by allowing prescribing of methadone, similar to how methadone is provided in Canada and many European countries.[43]

CONCLUSION

Patients with OUD encounter many challenges when hospitalized. This case illustrates how appropriate treatment of pain and withdrawal symptoms can reduce patient-directed discharges, why the term "AMA discharge" is problematic, and how to navigate barriers to discharge planning. Doing so can ensure humane and optimal clinical care for these patients.

Conflicts of Interest: The authors declare that they have no conflict of interest.

Ethical Approval: The authors declare that the case reported has adhered to relevant ethical guidelines, including obtaining consent from the patient discussed. As a case report does not meet DHHS definition of "research," the case report does not require IRB approval.

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