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OPIOIDS (D FIELLIN AND J DONROE, SECTION EDITORS)

Treatment of Opioid Use Disorder in the Acute Hospital Setting: a Critical Review of the Literature (2014–2019)

Melissa Weimer[1] · Kenneth Morford[1] · Joseph Donroe[1]

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Abstract

Purpose of Review Patients with opioid use disorder (OUD) often have concomitant medical conditions requiring hospitalization. This review describes the treatment of patients with OUD in acute care hospitals. Topics addressed include screening hospitalized patients for OUD, hospital initiation of medications for OUD (MOUD), Addiction Medicine Consult Services (AMCS), managing infectious complications of intravenous opioid use, and clinical innovations.

Recent Findings Management of opioid withdrawal and initiation of MOUD in hospitalized patients improves engagement in post-discharge addiction treatment. Implementation of an AMCS improves patient and provider outcomes. Care models that promote seamless transitions from the inpatient to outpatient setting for patients with OUD can improve patient outcomes and reduce health care utilization.

Summary Comprehensive addiction care for hospitalized patients with OUD improves patient, provider, and health care outcomes. Future studies should define the essential components of this integrated care and establish a new standard for the hospital care of patients with OUD.

Keywords Opioid · Addiction · Substance-related disorders · Hospital

Introduction

The incidence of opioid use disorder (OUD) and opioid overdose has increased significantly over the last 20 years requiring a broad response from health systems, government agencies, and the addiction treatment community [1]. In parallel, hospitalizations related to OUD and its medical complications, such as opioid overdose and intravenous (IV)-drug associated infections, have risen by 64% since 2005 [2–7]. Patients with OUD can be hospitalized for other medical issues like asthma or diabetes whose treatment may be complicated by their addiction. The hospital, therefore, is an important site for the screening, engagement, and initiation or continuation of treatment for OUD.

Despite this, treatment of OUD remains limited in hospital settings where frontline providers feel underprepared to address addiction [8]. A sense of "mutual mistrust" has been described between physicians and hospitalized patients with OUD leading to medical care that avoids addressing OUD [9]. When OUD is identified, the common response is to obtain a social work consultation [10, 11]. Most medical providers, however, lack education in evidence-based treatments for OUD to address issues identified by the social work consultation, resulting in hospital and discharge plans without effective addiction treatment [5, 10–12]. Although addiction psychiatrists and addiction medicine physicians receive specialty training to treat patients with substance use disorders, the workforce is scarce and usually limited to the outpatient setting [13]. This is compounded by misunderstandings about federal and state regulations for the provision of medications for opioid use disorder (MOUD), limiting their broad utilization in hospitalized patients.

To address these gaps in care, strategies of addiction care delivery are emerging within hospitals to support the growing

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✉ Melissa Weimer
melissa.weimer@yale.edu

Kenneth Morford
kenneth.morford@yale.edu

Joseph Donroe
joseph.donroe@yale.edu

[1] Department of Medicine, Yale University, 367 Cedar Street, Suite 305, New Haven, CT 06510, USA

number of patients with OUD. This review adds to current best practice reviews [14, 15] by highlighting hospital-based strategies for the initiation of treatment of OUD and its complications and safe transitions at hospital discharge.

Methods

We performed a literature search of peer-reviewed articles on OUD screening, diagnosis, and treatment in the acute hospital setting published between January 2014 and April 2019. We searched the MEDLINE database for the following search terms in various combinations: "substance-related disorders," "addiction," "opioid," "consult," "hospital," "buprenorphine," "methadone," and "naltrexone." Articles were also identified by searching through reference lists of included peer-reviewed literature. We included all study types. We limited our search to adult (> 18 years) hospitalized patients and excluded literature focusing on the emergency department (ED) only. We excluded non-English language articles. We followed the statement on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for RCTs (PRISM) for reporting our findings (Fig. 1) [16].

Results

A total of 122 articles were screened for eligibility. Ninety-three articles were excluded because they did not meet inclusion criteria primarily due to focusing on non-hospitalized patients and on substances other than opioids. A total of 46 articles were included for analysis. We organized the literature review findings into the following broad topics: screening patients for OUD, initiation of MOUD, Addiction Medicine Consult Services, treating OUD in patients with serious infectious complications, transitions of care, overdose prevention and harm reduction, and clinical innovations. See Table 1 for a summary of included articles with key outcomes.

Screening Hospitalized Patients for OUD

Screening tools for OUD have not been validated for the hospital setting. Despite this, current practice supports screening and many states now require it. A reasonable screening tool to use is the single-item screening question (SISQ) for drug use as part of every inpatient admission ("How many times in the past year have you used an illegal drug or used a prescription medication for non-medical reasons [for example, because of the experience or felling it caused]?") [37]. If positive for opioid use, providers should utilize the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria for OUD to establish the diagnosis [38].

No studies were identified that specifically address implementation of screening, brief intervention, and referral to treatment (SBIRT) for opioid use in the hospital setting. Evidence for the use of SBIRT for opioid use is limited to the ED and ambulatory setting and there is no evidence for its efficacy as a standalone intervention for drug use [39–41].

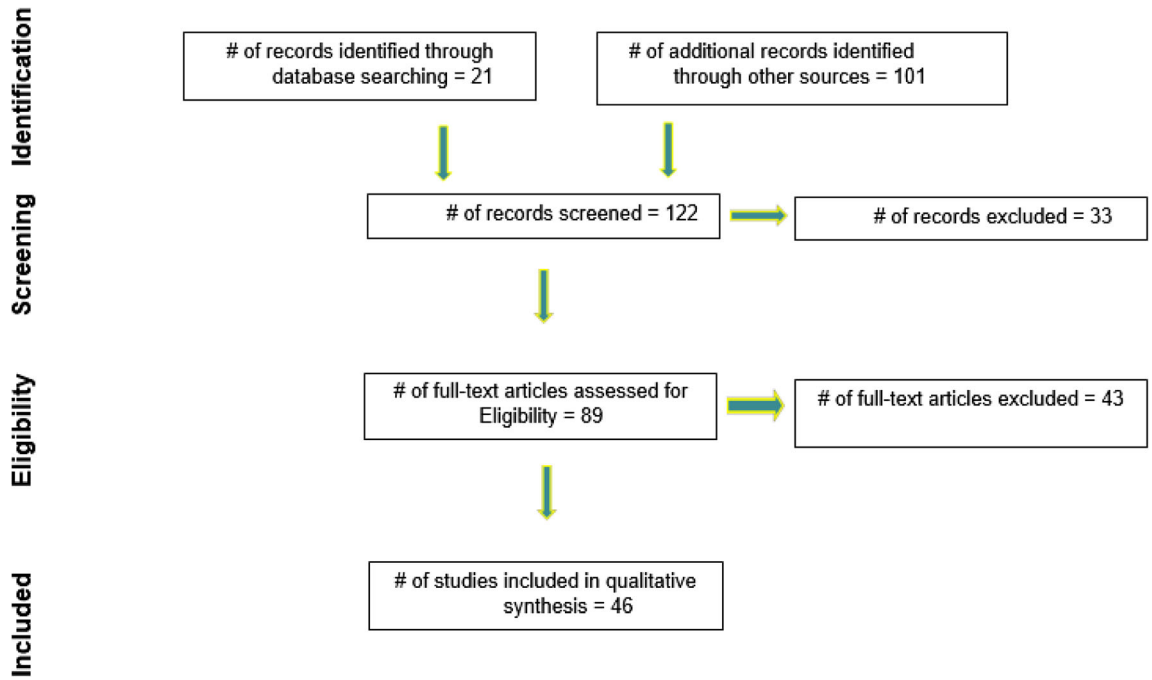

Fig. 1 Study identification, screening, eligibility, and inclusion

Table 1 Summary of studies

Reference	Study design	Participants	Intervention	Outcome measures	Results
Liebschutz, 2014 [17••]	RCT, Academic urban hospital	139 hospitalized patients with OUD	Randomize patients to 5-day buprenorphine detox vs in hospital induction on buprenorphine and linkage to ongoing maintenance care at discharge	Primary Entry into buprenorphine treatment within 6 months of enrollment Length of self-reported illicit opioid use at 1, 3, and 6 months	*Primary outcomes* **Detox group** -11.9% entered treatment -3% remained in treatment at 6 months *Linkage group* -72.2% entered treatment ($p < .001$) -16.7% remained in treatment at 6 months (p.007) *Secondary outcomes* **Detox group** -9% report no opioid use **Linkage group** -37.5% report no opioid use -IRR for opioid use 0.60;95% CI 0.46–0.73; $p < 0.01$
Lee, 2017 [18]	RCT, secondary analysis	72 hospitalized patients with OUD started on buprenorphine in the hospital	Start buprenorphine and link to ongoing care post-discharge	Predictors of entry into and retention in buprenorphine treatment	*Predictors of entry into treatment post-discharge:* Prior buprenorphine treatment (AOR 3.5, 95% CI 0.41, 29.65) Increased length of stay (OR 2.37, 95% CI 0.11; 50.92) PTSD symptoms (OR 1.85, 95% CI 0.50, 6.89) *Predictors of treatment engagement* Age (AOR 0.34, 95% CI − 0.10; 0.78) Non-Latino Caucasian (AOR 0.55, 95% CI − 0.25, 1.35) Prior buprenorphine treatment (AOR 0.52, 95% CI − 0.16, 1.19)
Cushman, 2016 [19]	RCT, secondary analysis	51 patients initiated on buprenorphine in the hospital vs 62 patients who underwent a buprenorphine taper in hospital	Randomize patients to buprenorphine detox vs in hospital induction on buprenorphine and linkage to care	Injection opioid use (IOU) frequency	*IOU frequency:* 1-month (IRR = 0.73, $p = 0.32$), 3-month (IRR = 1.20, $p = 0.54$), 6-month (IRR = 0.73, $p = 0.23$)
Suzuki, 2015 [20]	Case series	47 patients hospitalized with OUD	Initiation of buprenorphine treatment	Initiation of buprenorphine treatment within 2 months of hospital discharge	*Initiation of buprenorphine:* 22 (46.8%) patients initiated buprenorphine treatment within 2 months of discharge
Suzuki, 2016 [21]	Case series	29 patients hospitalized with OUD and infective endocarditis	Initiation of MOUD in the hospital	Initiation of MOUD in the hospital	*Initiation of MOUD* -9 (31%) initiated treatment with buprenorphine

Table 1 (continued)

Reference	Study design	Participants	Intervention	Outcome measures	Results
					-9 (31%) initiated treatment with methadone -11 (37.9%) declined MOUD
Moreno, 2019 [22]	Retrospective cohort study, urban academic medical center	470 patients with OUD who had received opioids in the hospital for 24 h	None	Predictors of 30- and 90-day hospital readmissions	*Hospital readmission* -85 (18%) readmitted -Median time to readmission was 26 days *Predictors of 30-day readmission* -Buprenorphine use at admission AOR 0.47 (95% CI 0.24, 0.93, *p* 0.03) -Median length of stay AOR 1.02 (95% CI 1.01, 1.05 *p* 0.05) *Predictors of 90-day readmission* -Heroin use AOR 0.59 (95% CI 0.37, 0.94, *p* 0.03) -Buprenorphine use at admission AOR 0.57 (95% CI 0.34, 0.96 *p* 0.03) -Medical admission: AOR 1.97 (95% CI 1.20, 3.25 *p* 0.0007) -Length of stay AOR 1.04 (95% CI 1.01, 1.06 *p* 0.003)
Trowbridge, 2017 [23••]	Case series, academic urban hospital	337 patients seen by AMCS	In hospital consult by AMCS (addiction medicine physician, RN with addiction experience, addiction medicine fellow)	Description of the initial implementation of the service	*Patient characteristics:* -78% opioid use disorder -37% alcohol use disorder -28% cocaine use disorder *Outcomes:* -75% of patients started on methadone linked to care -54%, 39%, 29% retained in treatment at 30, 90, 180 days -49% of patients started on buprenorphine linked to care -39%, 27%, 18% retained in treatment at 30, 90, 180 days
Wakeman, 2017 [24•]	Prospective, quasi-experimental design, urban academic center	265 patients seen by AMCS (86 patients with OUD)	In hospital consult by AMCS	-Change in Addiction Severity Index (ASI) -Illicit drug use 30 and 90 days after hospital discharge -Overdose (self-report)	*Mean ASI-drug at 30 days (not specific to OUD):* -Decreased 0.05 vs 0.02 in control group (*p* 0.003) *Mean ASI-drug at 90 days (not specific to OUD):*

Table 1 (continued)

Reference	Study design	Participants	Intervention	Outcome measures	Results
				-90-day health utilization (self-report)	-Decreased 0.05 vs 0.02 in control group (p 0.058) *Days abstinence at 30 days (self-report):* -Adjusted difference 2.59 $p = 0.02$ *Days abstinent at 90 days (self-report):* -Adjusted difference 1.70 $p = 0.21$ *Overdose at 30 days (self-report)* -Adjusted difference − 0.03 $p = 0.42$ *Overdose at 90 days (self-report)* -Adjusted difference 0.01 $p = 0.48$ *30-day health care utilization* *Hospitalizations* -61% vs 51% ($p = 0.001$) ED visits -66% vs 53% ($p = 0.002$)
Marks, 2018 [25••]	Case series, urban academic center	125 patients with infection related to IV opioid use, need > 2 weeks antimicrobial therapy, and not able to have outpatient antibiotic treatment	In hospital consult by AMCS	-Completion of parenteral antimicrobial therapy -Receipt of MOUD -Patients leaving AMA -90-day readmission	*Completion of parenteral antimicrobial therapy* 79% vs 40% $p < 0.0001$ *Receipt of MOUD* 87% vs 17% $p < 0.001$ *Patients leaving AMA* 16% vs 49% p 0.0003 *90-day readmission* HR 0.378 (95% CI 0.21, 0.69)
Reeve, 2016 [26•]	Case series, Australia	1615 patients with SUD	In hospital consult by AMCS	-Hospital readmissions -Costs	*Hospital readmissions* -39% fewer presentations *Cost* -Net benefit estimated to be $103,396/site
Nordeck, 2018 [27]	Case series, urban academic center	152 patients with OUD	In hospital consult by AMCS	Hospital readmission rates within 180 days Linkage to care	*Factors predictive of hospital readmission at 180 days* -OUD AOR 2.38 (95% CI 1.01, 5.61, $p = 0.047$) -Number of medical comorbidities AOR 1.20 (95% CI 1.06, 1.37, p 0.005) -Initiation of MOUD AOR 0.69 (95% CI 0.32, 2.02, p 0.64) *Linkage to care* -42% of patients initiated on MOUD vs 17% not initiated on MOUD ($p = 0.096$)

Table 1 (continued)

Reference	Study design	Participants	Intervention	Outcome measures	Results
Wakeman, 2017 [28•]	Survey, urban academic center	149 general internal medicine physicians	Inpatient addiction consult service, post-discharge addiction clinic, recovery coaches, SUD treatment within primary care	Change in general internists' attitudes, clinical practice, and preparedness post-intervention	-Preparedness to screen for SUD 27% vs 9% -Preparedness to diagnose SUD 23% vs 9% -Preparedness to deliver brief intervention 16% vs 5% -Preparedness to refer to treatment 36% vs 14% -Preparedness to discuss medication treatment 22% vs 5% -Preparedness to discuss overdose prevention 33% vs 5% -Preparedness to discuss harm reduction 22% vs 7% -Likelihood to prescribe naloxone 11% vs 0% -Likelihood to prescribe medication treatment 15% vs 2% -Likelihood to provide addiction treatment 18% vs 5%
Rodger, 2018 [29]	Case series, 3 hospitals, Canada	202 patients who injected drugs and had their 1st episode of infective endocarditis, 19 patients (9%) with OUD	None	Mortality	*Mortality in patients referred to addiction treatment* AOR 0.29 (95% CI 0.12, 0.73 p 0.008)
Fanucchi, 2018 [30]	Randomized, parallel study, academic hospital	20 patients with OUD, injection related infection	Randomized to usual care in hospital with buprenorphine vs early discharge with IV catheter, buprenorphine treatment, and close outpatient follow-up	-Days illicit opioid use in 12-week outpatient phase -Length of stay -Completion of IV antibiotics -Days of injection drug use	*Self-report days illicit opioid use and IV drug use in 12-week outpatient phase* -significant decrease both groups $p < 0.05$ *Length of stay* -45.9 (usual care) vs 22.4 (early discharge) $p < 0.001$ *Completion of IV antibiotics* -100% (usual care) and 100% (early discharge)
Rolfe, 2017 [31]	Case series, academic hospital	37 patients pre-intervention, 34 patients post-intervention All patients with IV drug use and need for prolonged antibiotics	9-point risk assessment by the IVAT	Median length of stay Readmission rates Leaving hospital AMA	*Median length of stay* 42 days pre; 18 days post $p < 0.001$ *Readmission rates* 51.4% pre; 32.4% post p 0.10 *Leaving hospital AMA* 13.5% pre; 23.5% post p 0.28
Eaton, 2019 [32]	Case series, academic hospital	37 patients pre-intervention 99 patients post-intervention	9-point risk assessment by the IVAT	Median length of stay Cost of care	*Median length of stay* 42 days pre; 22 days post *Cost of care*

Table 1 (continued)

Reference	Study design	Participants	Intervention	Outcome measures	Results
		All patients with IV drug use and need for prolonged antibiotics			$38,716 vs $26,014 (33% lower)
Englander, 2019 [33]	Case series	45 patients with SUD needing >2 weeks of IV antibiotics	Receiving OPAT at a MERT program	Acceptance of MERT Completion of Antibiotics	*Acceptance of MERT antibiotic treatment vs hospital treatment* -7 accepted vs 20 declined *Completion of antibiotics* -3 (43%)
Beieler, 2016 [34]	Case series	53 patients, 53% with current IV drug use, needing prolonged IV antibiotics	Receiving OPAT, addiction treatment and harm reduction	Successful completion of OPAT Successful completion of antimicrobial course for specific diagnosis Readmission rate Cost saving	*Successful completion of OPAT* -34 (64%) completed *Successful completion of antimicrobial course* -46 (87%) completed *Readmission rate* 30% *Cost saving* $25,000 per episode of OPAT
Jafari, 2014 [35]	Case series, community setting, Canada	165 patients needing OPAT, 65% with OUD	CTCT, offering medical care, antibiotics, and addiction treatment for patients who need OPAT	Leaving AMA Patient satisfaction	*Leaving AMA* 1.2% of patients *Patient satisfaction* 100% favor care in CTCT vs hospital
Fanucchi, 2018 [36]	Randomized, parallel group study, academic medical center	20 adult patients, infection-related infection, OUD, desiring buprenorphine	Randomized to usual care (completing IV antibiotics in the hospital) vs early discharge with PICC and treatment with buprenorphine	Completion of IV antibiotics Length of stay	*Completion of IV antibiotics* Usual care 100% vs 100% treatment group *Length of stay* Usual care 45.9 days vs 22.4 days treatment group ($p < 0.001$) *Outpatient IV antibiotic days* Usual care 1.8 days vs 20.1 days treatment group ($p < 0.001$)

Abbreviations: *RCT*, randomized controlled trial; *OUD*, opioid use disorder; *MOUD*, medication for OUD; *ACMS*, Addiction Medicine Consult Service; *AMA*, against medical advice; *SUD*, substance use disorder; *IV*, intravenous; *IVAT*, Intravenous Antibiotics and Addiction Team; *MERT*, medically enhanced residential treatment; *OPAT*, outpatient parenteral antibiotic therapy; *CTCT*, Community Transitional Care Team; *PICC*, peripherally inserted central catheter

Hospital-Initiated Medication for Opioid Use Disorder

Buprenorphine, methadone, and extended-release naltrexone are the three medications approved by the Food and Drug Administration (FDA) for the treatment of OUD in the United States (U.S.). Although federal regulations in the U.S. restrict the prescription and administration of buprenorphine and methadone in the outpatient setting, these regulations are not applicable to the hospital setting. Title 21 of the Code of Federal Regulations section 1306.07 C imposes no limitations on a hospital medical provider to prescribe buprenorphine or methadone for the treatment of opioid withdrawal or OUD to a hospitalized patient who has been admitted for an acute medical condition other than OUD [42, 43]. Additionally, hospital providers do not need a Drug Enforcement Agency (DEA) waiver to prescribe buprenorphine to patients with OUD in the hospital. Therefore, both methadone and buprenorphine can be used to treat acute opioid withdrawal to facilitate inpatient medical care and/or used to initiate ongoing treatment of OUD [42]. Despite this, uptake of this practice remains low in most hospitals [44].

Studies support that hospitalized patients with OUD are receptive to starting MOUD and that hospital-initiated MOUD can improve engagement with addiction treatment after discharge and reduce readmission rates [20–22, 45]. In the last 5 years, one RCT, one retrospective cohort study, and two case series evaluated hospital-initiated MOUD [17••, 18, 19, 22]. Three studies highlight that hospitalized patients with OUD who initiated buprenorphine were more likely to be engaged in addiction treatment at 2 and 6 months [17••, 18, 19]. Importantly, Liebschutz et al. demonstrated that hospitalized patients who started buprenorphine treatment were significantly more likely to engage with outpatient OUD treatment and 40% less likely to use illicit drugs 6 months post-discharge compared with patients randomized to a buprenorphine detoxification protocol (IRR 0.60; 95% CI 0.46–0.73; $p < 0.01$) [17••]. However, retention in treatment at 6 months was overall quite low for patients in the linkage group [17••]. Finally, a retrospective cohort study showed that although patients with OUD had high readmission rates at 30 and 90 days, hospitalized patients treated with buprenorphine had a 50% and 43% reduction in readmission risk at 30 and 90 days, respectively [22].

Addiction Medicine Consult Service

With nearly 10% of hospitalized patients admitted with a condition directly or indirectly related to OUD, it is imperative to have trained medical providers available to identify, manage, and treat OUD [46]. Previous authors have described hospitalization for patients with OUD as a "teachable" and "reachable" moment [42, 45, 47, 48]. A paradigm of hospital-based addiction care called the Addiction Medicine Consult Services (AMCS) has grown over the last 40 years to engage this highly vulnerable hospitalized patient population [45, 49, 50]. A recent review compares the various AMCS models as of 2019 and summarizes our current understanding of their outcomes [51]. Additionally, a large trial is underway in the New York City Health System to inform ongoing practice and evidence for AMCS [52].

AMCS Structure

Few studies elucidate the most effective structure of the AMCS. One case series details the planning, design, and implementation of an AMCS called IMPACT (Improving Addiction Care Team) in an academic health system based on a needs assessment of key stakeholders [48]. It included a model of hospital-based addiction care designed to maximize engagement and trust building with patients and offer open access for post-hospital discharge OUD treatment [48]. IMPACT mapped its intervention around these priorities and created a specialized multidisciplinary team with community partnerships to engage hospitalized patients with OUD at various stages of change, treat opioid withdrawal, and refer to ongoing OUD treatments after hospitalization [48]. A mixed-methods study described that most AMCS programs in the United States are similarly interprofessional and focus their clinical services on OUD assessment, withdrawal management, initiation of MOUD, and seamless linkage to care [51]. The essential composition of an AMCS for optimal patient outcomes is not known; however, it is generally agreed that an interprofessional team with addiction expertise that includes physicians, nurses, advanced practice providers, social workers, pharmacists, and peers is effective [51, 53•]. Additionally, there may be benefit to co-staffing an AMCS with providers trained in psychiatry and internal medicine who work collaboratively to optimize patient outcomes [54]. A practical toolkit based on the IMPACT experience was developed to help other health systems implement an AMCS [53•]. A similar toolkit is also freely available online at www.projectshout.org.

Patient-Related Outcomes

Five descriptive studies evaluated the effect of the AMCS on a variety of patient outcomes including initiation of MOUD, addiction severity, opioid abstinence, opioid overdose, completion of hospital treatment, hospital readmission rates, and cost of care [23••, 24•, 25••, 26•, 27]. Most studies focus on decreased hospital readmission rates for patients with OUD [24•, 25••, 26•]. A large study in Australia demonstrated that patients with substance use disorders (SUD) seen by the AMCS had 39% fewer hospital readmissions compared with patients with SUD not seen by AMCS and the net cost benefit of the AMCS was estimated to be $103,296 (Australian

dollar)/per site [26•]. Significant reductions in hospital readmissions and ED visits after involvement of the ACMS were demonstrated in two other studies at both 30 days and 90 days post-hospitalization, including a nearly 60% reduction in readmission risk in patients with OUD requiring prolonged intravenous (IV) antibiotics [24•, 25••]. In that same study, patients with OUD seen by the AMCS were also more likely to complete IV antibiotics (79% vs 40%, $p < 0.001$), more likely to receive MOUD (87% vs 17%, $p < 0.001$), and less likely to leave the hospital against medical advice (AMA) (16% vs 49%, p 0.0003) [25••]. Of the many factors correlated with hospital readmission, initiation of MOUD by an AMCS correlated with a 31% (AOR 0.69 (95% CI 0.32, 2.02 p 0.64)) reduction of readmission risk at 180 days post-discharge [27].

One case study evaluating linkage to care outcomes showed that 75% of hospitalized patients with OUD initiated on methadone by an AMCS presented for ongoing methadone treatment post-discharge, and 54%, 39%, and 29% were retained in treatment at 30, 90, and 180 days, respectively [23••]. Of those patients initiated on buprenorphine by the AMCS, 49% presented for buprenorphine treatment post-discharge and 39%, 27%, and 18% were retained in treatment at 30, 90, and 180 days, respectively [23••].

The effect of AMCS compared with no AMCS intervention on addiction severity and self-reported opioid use was described in one study which showed significant reductions in the mean Addiction Severity Index at 30 and 90 days post-discharge, but found no significant differences in self-reported opioid abstinence or opioid overdose at 30 and 90 days [24•]. A qualitative study of hospitalized patients with OUD described the benefits of AMCS on patients [55]. Patients in the study stated that they valued access to life-saving MOUD and coordination of addiction care post-discharge, though acknowledged that hospitals alone are unlikely to adequately address complex life stressors and trauma [55].

Provider-Related Outcomes

The effect of AMCS on hospital staff cannot be understated. Three qualitative studies described how the creation of an AMCS can be a "sea change" for a health system [28•, 47•, 55]. AMCS can positively influence providers' attitudes, beliefs, and experiences, as well as reduce provider burnout and improve preparedness when caring for patients with OUD [8, 47]. In one study, prior to the creation of the AMCS, hospital providers described medical care for patients with OUD as "chaotic" and leading to feelings of "moral distress" [47]. The AMCS helped "reframe addiction as a chronic disease, improving patient engagement and communication and humanizing care" [47].

Serious Infectious Complications of Injection Opioid Use

Use of unsterile injection equipment, contaminated drugs or fillers, use of unsterile water or saliva in drug preparation, and needle licking habits are some of the practices that contribute to injection drug-related bacterial infection [56]. Hospitalization rates, length of stay, and health care costs have risen in parallel with the increased incidence of injection opioid use and its complications [2].

Management of Patients with Injection Drug Use–Related Infective Endocarditis

Though all infectious complications of IV opioid use are serious, infective endocarditis (IE) can be one of the most complicated and morbid with high rates of hospital admission and reinfection [57]. The incidence of IE among people who inject drugs (PWID) is 100 times higher than the general population and hospitals have seen a steady rise in cases of injection drug use–related infective endocarditis (IDU-IE) over the last 20 years [5, 58–60]. A study of the Health Care and Utilization Project National Inpatient Sample (HCUP-NIS) dataset showed that hospitalizations related to IDU-IE increased from 7 to 12.1% between 2000 and 2013 [59]. During this timeframe, rates of IDU-IE increased the most among PWID who are younger, non-Hispanic white, and from rural areas [59, 61]. Health care–related costs and hospital length of stay are also higher for patients with IDU-IE and exceed that of other medical conditions [2, 5, 48, 61]. Additionally, long-term outcomes for patients with IDU-IE are poor in the absence of integrated addiction treatment resources. A recent study demonstrated that compared with patients with non-IDU-IE, patients with IDU-IE had higher long-term mortality (HR 2.2, 95% CI 1, 4.8, $p = 0.04$) related to opioid relapse [62].

In 2016, the American Association for Thoracic Surgery created a consensus guideline for the surgical treatment of IE and provided the following recommendation, "Normal indications for surgery are reasonable to apply to patients who [use] intravenous drug[s]. Decision-making must take the addiction into account, and management must include treatment of addiction" [63]. A recent case series has shown that referral to addiction treatment in patients with their first episode of IDU-IE is associated with lower mortality rate (HR 0.29; 95% CI 0.12, 0.73; $p = 0.008$) [29]. Despite a recognition that treatment for addiction should be part of the care provided to patients with IDU-IE and patients with IDU-IE report interest in addiction treatment, very few patients with OUD and IE receive treatment in the hospital [5, 10, 11, 30]. Patients and providers agree that the current health system is not equipped or designed to address the complex care for patients with IDU-IE [62, 64]. In the absence of effective treatment models, some

surgeons have developed "contracts" for their patients with IDU-IE to sign and agree to no longer use IV opioids [65]. These models ignore the central role MOUD can play to prevent or reduce ongoing opioid use and operates with the misunderstanding that addiction is a choice and patients can abstain through willpower alone [66]. Newer models of care such as the AMCS help reframe addiction as a chronic disease and deliver appropriate addiction treatments to patients in the hospital, though robust evidence for the beneficial effect of the AMCS for this specific patient population is lacking.

Strategies to Provide Prolonged Antibiotics in Patients with OUD and Severe Bacterial Infections

Three studies evaluated novel post-discharge treatment settings for provision of antibiotics and two studies describe outcomes of outpatient parenteral antibiotic therapy (OPAT) in PWID to determine the effectiveness of different strategies for treatment of serious bacterial infections associated with injecting (e.g., osteomyelitis, septic arthritis, or endovascular infections) and need for prolonged parenteral antibiotics [31, 33, 34•, 35, 36]. Building on research demonstrating that patients discharged to a residential addiction treatment program with nurse-administered parenteral antibiotics complete antibiotics and is cost saving [67], one study described a post-hospital discharge outpatient program called the medically enhanced residential treatment (MERT) that administered parenteral antibiotics in a residential addiction treatment setting via OPAT with MOUD [33]. Use of MERT was limited due to patient ambivalence towards residential treatment and concerns about prioritizing physical health needs, high demands of residential treatment, and the perception that MERT patients "stood out" as "different" by addiction treatment staff and residents. Consequently, MERT ended after 6 months, highlighting the challenges of successfully implementing such a program [33]. Two other studies described interventions offering parenteral antibiotics via OPAT, addiction treatment, and housing through medical respite programs [34•, 35]. Both described high rates of antibiotic completion and one demonstrated cost savings of $25,000 per patient episode of OPAT [34•].

Home-based OPAT is another strategy to safely provide prolonged parenteral antibiotics to patients with OUD who are discharged home [31, 32, 36]. One study described a novel hospital-based program called the Intravenous Antibiotics and Addiction Team (IVAT) which utilizes a nine-point risk assessment tool to determine which patients with OUD can be safely offered OPAT at home vs remaining in the hospital for the duration of antibiotic treatment. The IVAT model, though not specifically designed to offer addiction treatment to PWID, reduced median length of hospital stay (42 days vs 18 days, $p < 0.001$) and cost of hospital care ($38,716 vs $26,014) [31, 32]. However, IVAT did not improve readmission rates or the number of patients leaving the hospital AMA [31, 32]. Finally, a study presented as a poster presentation at the 2018 College on Problem of Drug Dependence randomized 20 patients with OUD and IV drug-related infection to receive usual hospital care with parenteral antibiotics along with buprenorphine treatment compared with early discharge from the hospital with OPAT and outpatient buprenorphine treatment [36]. Preliminary findings demonstrate 100% completion of parenteral antibiotics for both groups, a decrease in self-reported illicit opioid use for both groups, and a reduction in length of hospital stay for patients in the early hospital discharge/OPAT group (22.4 days vs 45.9 days, $p < 0.001$) [36]. If successful on a larger scale, this model could help reduce health care costs associated with serious bacterial infections in patients with OUD while not compromising outcomes. Further investigation into these strategies is warranted to develop safe, effective, and cost-saving measures for patients with OUD who need prolonged parenteral antibiotics.

Transitions of Care

Transitions of care from the inpatient to outpatient setting represent a critical and challenging step in effectively caring for individuals with OUD. As previously described, hospital-initiated MOUD is associated with improved linkage to ongoing outpatient treatment [17, 45]. However, restricted access to outpatient methadone and buprenorphine treatment in the United States poses a barrier to initiating MOUD in the hospital setting [68]. Furthermore, retention in care remains a challenge, with retention rates substantially lower at 6 months post-hospital discharge [23].

Several models of care have been developed to improve linkage to outpatient OUD treatment. Aptly named "bridge" clinics provide short-term MOUD for patients discharged from hospital settings while seeking to establish long-term treatment [15]. The Boston Medical Center established a once-weekly discharge clinic for patients seen by their AMCS to provide ongoing treatment pending admission to permanent outpatient addiction treatment and found high rates of initial engagement with treatment post-hospital discharge [23].

Community partnerships play a crucial role in improving transitions of care. The aforementioned AMCS called IMPACT worked diligently during its planning and development phases to engage community stakeholders such as community-based SUD treatment partners, skilled nursing and criminal justice representatives, and hospital leadership to coordinate post-hospital SUD care pathways [53]. By enhancing collaboration across organizations and creating a novel team member called an "In-reach counselor" who bridged the gap between the hospital and community treatment, IMPACT coordinated post-hospital linkage plans to formal (e.g., opioid treatment program) or informal (e.g., alcoholics anonymous) SUD treatment for 75% of patients seen by the service during its first 3 years of operation [53].

Overdose Prevention and Harm Reduction

The acute hospital setting offers an opportunity to provide harm reduction interventions for patients with OUD. PWID represent a particularly vulnerable group and have significantly higher drug-related mortality in the 28-day period following hospital discharge compared with those without injection use of any drug [69]. A study of PWID who left the hospital AMA suggested that hospital-based harm reduction efforts would promote patient-centered care [70]. While community-based harm reduction interventions such as overdose education and naloxone distribution have been shown to be cost-effective and to reduce opioid overdose death rates, no studies were identified that specifically examine the integration of harm reduction strategies in acute hospital settings [71, 72]. Thus, recommendations for harm reduction during hospitalization are based on expert opinion.

Two narrative reviews present clinical checklists to optimize the health and safety of PWID prior to hospital discharge [73, 74]. Strategies to address overdose prevention in hospitals include initiating MOUD, providing opioid overdose education, and prescribing naloxone upon discharge [73]. Harm reduction strategies should encourage the use of non-stigmatizing language and consider involving people with lived experience (i.e., recovery peer) in clinical care [74]. Inpatient settings also offer a chance to develop overdose prevention plans that include safety steps such as not mixing opioids with other sedatives, using opioids in the presence of others, and using a small tester amount of opioid to assess drug potency [73]. Strategies to address infection prevention include reviewing safer injection techniques; screening for sexually transmitted infections, hepatitis, and tuberculosis; evaluating the need for vaccination against hepatitis A and B, tetanus, influenza, and pneumococcus; and initiating pre-exposure prophylaxis (PrEP) for HIV [73]. Interventions with solid evidence in community settings but require further investigation for implementation in hospitals include prescribing oral and IV opioids to inpatients who have not responded to conventional MOUD, providing sterile drug use equipment, and standardizing safe discharge protocols for PWID leaving AMA [74].

Clinical Innovation: New Buprenorphine Induction Approaches in the Hospital Setting

Induction to buprenorphine is a straight forward process but can be challenging when transitioning hospitalized patients from long-acting full opioid agonists like methadone due to hospital length of stay constraints and acute medical complexity. Two methods have been proposed to reduce the opioid-free withdrawal period of 12–48 h required to avoid precipitated withdrawal during buprenorphine induction, particularly when transitioning from a highly potent full agonist such as methadone. The first, described in a case report, uses a 5-day transdermal fentanyl bridge rather than a methadone taper to transition a patient from 30 mg of daily methadone to buprenorphine [75]. The second method utilizes a new approach called "microdosing" of buprenorphine [76–78]. With this approach, patients are transitioned from full agonist opioids to buprenorphine with the concomitant use of very low doses of buprenorphine. Utilizing this method, patients described mild opioid withdrawal symptoms and were otherwise able to transition more quickly [76–78].

Clinical Innovation: Acute Pain and Perioperative Management

Acute pain treatment in patients with OUD can present a clinical challenge due to opioid tolerance, possible concomitant opioid or other substance withdrawal, and patient fear of inadequate analgesia. To date, no randomized controlled trials have evaluated pain treatments for patients with OUD on MOUD. In general, multimodal pain treatment is recommended to effectively treat perioperative pain and reduce overall opioid use [79]. For patients prescribed methadone treatment, methadone can be continued at current doses and concurrent full agonist analgesics along with non-opioid treatments can be provided. A more complex issue and one where the field is evolving involves treating patients with acute pain who are prescribed buprenorphine. In 2004, the US Center for Substance Abuse Treatment (CSAT) recommended that patients prescribed buprenorphine for OUD should discontinue buprenorphine if a full opioid agonist is prescribed [80]. This recommendation led to the widespread practice of discontinuing buprenorphine prior to surgery. That blanket recommendation is now reconsidered as many addiction specialists have observed negative outcomes such as poorly controlled pain, active opioid withdrawal, and high rates of relapse in patients with OUD who were previously stable on buprenorphine [81]. Current recommendations suggest considering two approaches for perioperative management of patients prescribed buprenorphine: discontinuing buprenorphine or continuing buprenorphine [79, 81]. Expert opinion currently favors continuing buprenorphine and only discontinuing buprenorphine when adequate analgesia is not achieved [81]. The rational for continuing buprenorphine during episodes of acute pain is supported by data showing positron emission tomography activity at the mu receptor for buprenorphine-maintained patients exposed to carfentanil [82, 83]. A recent commentary offers a perioperative protocol for continuation of buprenorphine (see Fig. 2) [82]. The protocol recommends continuation of buprenorphine at a dose of 12 mg or less, multimodal analgesia, regional anesthesia, and full opioid agonists when necessary and appropriate for a defined period to control pain and then return to preoperative

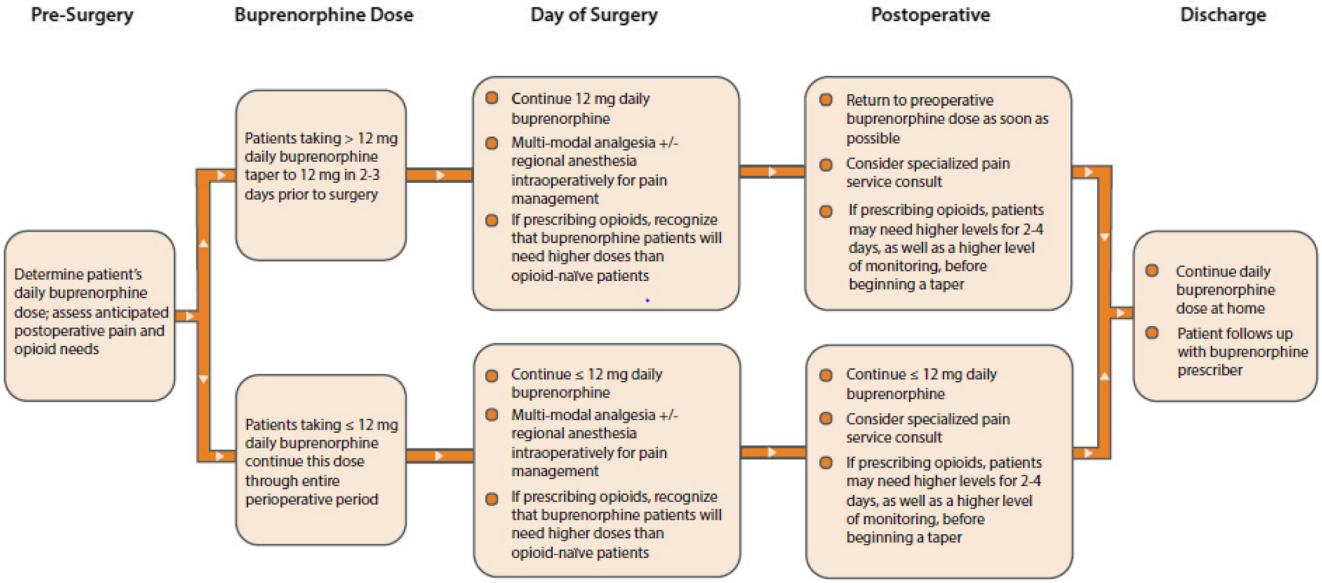

Fig. 2 Perioperative buprenorphine protocol from Lembke et al. [82]

buprenorphine dose when possible [82]. Other options to achieve analgesia with buprenorphine include dividing the patient's usual dose to twice or three times a day [81]. If buprenorphine is discontinued prior to surgery, providers will need to manage opioid withdrawal symptoms in addition to providing medications for perioperative analgesia.

Conclusions

The number of hospitalizations for people with OUD is growing in parallel with the increasing prevalence of OUD in the United States. Challenges to delivering high-quality care for people with OUD in the hospital setting include low levels of hospital provider comfort with initiating and managing MOUD, the importance of treating OUD concurrently with other acute medical conditions such as injection related infections, and providing safe transitions of care at the time of hospital discharge. None-the-less, hospitalization is both a "reachable" and "teachable" moment. "Reachable" in the sense that patient motivation for treatment is often high and medical providers, mental health specialists, and social workers are more accessible than in most outpatient settings. "Teachable" in the sense that both patients and providers have opportunities to learn from one another about improving care for OUD.

While it is on the shoulders of frontline staff to carefully screen and identify hospitalized patients with OUD, the available evidence informs us that a multidisciplinary, coordinated approach is needed to optimize outcomes when treating patients with OUD in the hospital setting. The AMCS is emerging as one model of delivering such multidisciplinary care. Research supports that when AMCS guides the care of patients with OUD, both patients and providers benefit. Patients are more likely to receive evidence-based addiction treatment and harm reduction interventions, to transition to outpatient addiction care, and to complete parenteral antibiotic therapy for IV drug use–related infections [23••, 25••, 27]. Patients with OUD are less likely to leave the hospital AMA or require hospital readmission [25••, 26•, 27]. Providers working with the AMCS learn skills to improve their treatment of patients with addiction, are more likely to provide naloxone at hospital discharge, and less likely to be frustrated by difficult provider-patient interactions [8, 47]. Future research should continue to evaluate the impact of AMCS on important clinical outcomes such as discharges AMA, hospital readmissions, length of hospital stay, management of IV drug use–related infections, and the economic impact of AMCS on health systems.

For health systems that do not have resources for an AMCS, more research into optimizing multidisciplinary care delivery for hospitalized patients with OUD is needed. Ultimately, through more education and experience, the goal is for hospital providers to offer the same high-quality care to people with OUD as they do for people with other complex medical conditions such as diabetes and cirrhosis, with the highest complexity patients with OUD remaining in the domain of the addiction specialist. Importantly, as hospital-based interventions to improve care delivery to people with OUD evolve, interventions to improve access to high-quality outpatient addiction treatment resources must evolve in parallel.

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Compliance with Ethical Standards

Conflict of Interest Melissa B. Weimer reports one-time personal fees from Alkermes and Indivior, outside the submitted work.

Kenneth Morford has no conflicts of interest to declare.

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- •• Of major importance

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