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Journal Title: AIDS (London, England)
Volume: Volume 37, Number 12
Publisher: Lippincott Williams & Wilkins | 2023-10-01, Pages 1799-1809
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.1097/QAD.0000000000003629
Permanent URL: https://pid.emory.edu/ark:/25593/w854h

Final published version: http://dx.doi.org/10.1097/QAD.0000000000003629

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Accessed January 5, 2024 5:14 PM EST
Undertreatment of opioid use disorder in patients hospitalized with injection drug use-associated infections

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\textbf{Objective:} To evaluate the association between medication for opioid use disorder (MOUD) initiation and addiction consultation and outcomes for patients hospitalized with infectious complications of injecting opioids.

\textbf{Method:} This was a retrospective cohort study performed at four academic medical centers in the United States. The participants were patients who had been hospitalized with infectious complications of injecting opioids in 2018. Three hundred and twenty-two patients were included and their individual patient records were manually reviewed to identify inpatient receipt of medication for opioid use disorder (MOUD), initiation of MOUD, and addiction consultation. The main outcomes of interest were premature discharge, MOUD on discharge, linkage to outpatient MOUD, one-year readmission and death.

\textbf{Results:} Three hundred and twenty-two patients were predominately male (59\%), white (66\%), and median age 38 years, with 36\% unstably housed, and 30\% uninsured. One hundred and forty-five (45\%) patients received MOUD during hospitalization, including only 65 (28\%) patients not on baseline MOUD. Discharge was premature for 64 (20\%) patients. In the year following discharge, 27 (9\%) patients were linked to MOUD, and 159 (50\%) patients had at least one readmission. Being on MOUD during hospitalization was significantly associated with higher odds of planned discharge [odds ratio (OR) 3.87, \(P < 0.0001\)], MOUD on discharge (OR 129.7, \(P < 0.0001\)), and linkage to outpatient MOUD (OR 1.25, \(P < 0.0001\)), however, was not associated with readmission. Study limitations were the retrospective nature of the study so post-discharge data are likely underestimated.

\textbf{Conclusion:} There was dramatic undertreatment with MOUD from inpatient admission to outpatient linkage, and high rates of premature discharge and readmission.

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Received: 24 March 2023; revised: 6 June 2023; accepted: 12 June 2023.
DOI:10.1097/QAD.0000000000003629

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Engagement in addiction care during hospitalization is a critical first step in improving the care continuum for individuals with opioid use disorder; however, additional interventions may be needed to impact long-term outcomes like readmission.

Keywords: addiction, infectious complications of opioid use, opioid use disorder, serious injection-related infections

Introduction

The United States opioid epidemic has resulted in historic levels of overdose deaths and a parallel rise in infectious complications of injection opioid use [1,2]. Consequently, rates of hospitalization from infections because of injecting opioids have increased precipitously, resulting in costly hospitalizations with high morbidity and mortality for an otherwise young, healthy population [3–5].

Medication for opioid use disorder (MOUD) is an evidence-based strategy to treat opioid use disorder (OUD) by reducing craving and withdrawal, opioid use frequency, risk behaviors [6,7], and mortality [8]. Interest in initiation of MOUD is high among hospitalized patients [9] and inpatient initiation of buprenorphine has been shown to result in higher rates of linkage to outpatient treatment compared with detoxification and referral alone [10]. Despite this, rates of MOUD initiation among people hospitalized with infectious complications of injecting opioids remain remarkably low, often below 20% [11,12].

Among people who inject drugs (PWID), outpatient MOUD reduces incidence and improves outcomes of HIV and hepatitis C virus (HCV) [13–15]. However, the impact of inpatient initiation of MOUD on long-term outcomes of patients hospitalized with bacterial infections has not been well documented. A single-site retrospective study evaluating patients hospitalized with serious infections related to opioid use found that addiction consultation was associated with increased MOUD receipt, decreased premature discharge, and reduced 90-day readmission [16]. In contrast, in a retrospective cohort study of patients with OUD hospitalized with infective endocarditis or osteomyelitis, initiation of MOUD was not associated with rates of premature discharge or 30-day readmission [11]. Therefore, we lack a complete understanding of the impact of inpatient addiction interventions, including initiation of MOUD, on outcomes of patients hospitalized with infectious complications of OUD both during and after hospitalization.

The CHOICE study was a retrospective analysis of the continuum of care for patients hospitalized with infectious complications of opioid injection across four healthcare systems. We aimed to understand the association between MOUD initiation and addiction consultation on outcomes, including premature discharge, readmission, and postdischarge linkage to MOUD treatment.

Methods

Study design and patient population

The CHOICE Study (The Continuum of Care in Hospitalized Patients with Opioid Use Disorder and Infectious Complications of Drug Use) is a retrospective cohort study to describe the continuum of care for MOUD in persons with OUD who were hospitalized with an infectious complication of injection drug use (IDU). The study was conducted at four academic medical centers in the United States: the University of Maryland Medical System, The George Washington University Hospital, Emory University and Grady Memorial Hospitals, and the University of Alabama at Birmingham. The study was approved by the University of Maryland Institutional Review Board (IRB) and the University of Alabama at Birmingham IRB. Other sites relied on the University of Maryland as IRB of record.

Participants identification and inclusion

To meet inclusion for the study, patients had to be 18 years or older and hospitalized between 1 January 2018 and 31 December 2018. To identify participants, we queried electronic medical records (EMRs) at each site using International Classification of Diseases, Ninth or Tenth Revisions (ICD-9 or ICD-10) codes for OUD and one or more infections associated with IDU (see Protocol). Individual patient charts were then manually reviewed to verify that OUD was an active diagnosis during the 2018 sentinel admission, and that presumption of an IDU cause of infection was documented. Sentinel admission was defined as the first admission occurring in 2018 for an infectious complication of IDU within the hospital system.

Data collection

Using institution-specific EMRs, data were abstracted for baseline demographics and admission information, patient-level interventions during sentinel admission,
and transitions of care during the discharge process. Longitudinal outcomes were assessed for the 1-year period after sentinel admission. Study data were collected and managed using REDCap electronic data capture tools hosted at the University of Maryland [17,18].

**Medication for opioid use disorder status**
The primary variable of interest was MOUD (methadone or buprenorphine) receipt during sentinel admission. Patients were considered to be on ‘baseline MOUD’ if there was documentation of being on MOUD at the time of admission. For patients not on baseline MOUD, charts were reviewed to determine if and when MOUD was initiated during hospitalization.

Patients considered to be ‘on MOUD’ during hospitalization represent a combination of those on baseline MOUD continued during admission, and those not on baseline MOUD who were initiated during hospitalization. Patients were considered on MOUD only if MOUD was utilized for the purpose of OUD treatment, and not solely for pain or withdrawal management. Patients ‘not on MOUD’ during hospitalization represent a combination of those on baseline MOUD not continued during admission, and those not on baseline MOUD who were not initiated on MOUD during hospitalization. The analysis of patients who initiated MOUD while hospitalized vs. those who were not was restricted to patients not on baseline MOUD.

**Addiction consultation**
Patients were assessed for addiction consultation during sentinel admission, defined as a consultation for assistance with OUD management by a team with the capacity to prescribe MOUD. Patients were assessed for placement of consultation order and consultation completion – defined as completion of an initial consultation note.

**Hospital system resources**
From 2018 to 2019, one of the four sites had neither inpatient addiction consultation services, nor outpatient MOUD services. Of the three institutions with outpatient MOUD services in the study time period, one site had outpatient buprenorphine and methadone resources available within 24 h regardless of insurance status, one site had outpatient buprenorphine services that were grant supported and, therefore, free to all patients regardless of insurance status with appointments available within 24 h, and one had outpatient buprenorphine services for both insured and uninsured patients with an approximate 4-week waiting period.

**Outcome variables**
The main outcomes of interest were: premature discharge (also known as against medical advice or patient-directed discharge); MOUD on the discharge prescription list; linkage to outpatient MOUD – defined as attendance of one outpatient MOUD visit in the year after admission; readmission within 1 year; and death within 1 year. Assessment of hospital readmission included number of readmissions within the hospital system within 1 year and time to first readmission. Verification of MOUD visit attendance was limited to outpatient facilities included in site-specific health system EMRs. Outcomes were only assessed in patients who survived to discharge. Death and reason for death were assessed by chart review within the site-specific EMR.

**Statistics**
Bivariate analyses were conducted using chi-square test or Fisher exact test. For multivariable analysis, we used logistic regression for binary outcomes, and Poisson regression for the number of readmissions within 1 year. Variables controlled for in regression models included: race, gender, insurance status, housing status, infection severity, and stimulants in urine drug screen. Generalized estimating equation (GEE) was used to account for clustering of patients within each study site. Logistic regression with GEE was also used for comparing the completion rates of consultation orders. For assessment of exposure variables associated with linkage to outpatient MOUD, the site without outpatient MOUD services during the study period was excluded. For assessment of outcomes associated with addiction consultation (discharge status, MOUD on discharge, and readmission), a sensitivity analysis was completed excluding the site that lacked addiction consultation. SAS version 9.4 (SAS Institute, Cary, North Carolina, USA) was used, and all P values are two-sided.

**Results**

**Patient inclusion**
A total of 1285 patients were initially identified with ICD-9/10 codes for OUD and infection of whom 322 (25%) met inclusion criteria and had full data collected (Fig. 1).

**Demographics and baseline admission information**
The final cohort (n = 322) was predominately men (59%), white (66%), and median age 38 (Table 1). Of note, 36% were unstably housed, and almost a third of patients (30%) were uninsured.
Injection drug use-associated infectious diseases and antimicrobial therapy

Nearly half of the cohort (47%) had exclusively a skin and soft tissue infection, whereas 53% had a more serious infection with or without a skin and soft tissue infection. Intravenous antibiotics were prescribed for 73% of patients (Table 2).

Medication for opioid use disorder

Ninety-three (29%) patients were on baseline MOUD (68 methadone; 25 buprenorphine), of whom 86% were continued on MOUD during hospitalization (Fig. 2). Of the 229 (71%) individuals not on baseline MOUD, 28% were initiated on MOUD (54 buprenorphine; 11 methadone) a median of 3 days (IQR 1–6) after admission. MOUD initiation was significantly associated with having an addiction consultation vs. not (53.2 vs. 5.8%, \(P < 0.0001\)). In total, 145 (45%) patients received MOUD at some point during hospitalization (Table 2).

Inpatient consultations

An addiction consultation was completed for 143 (44%) patients. When ordered, addiction consultations were significantly less likely to be completed (79%) than infectious diseases (96%, \(P < 0.0001\)), psychiatry (92%, \(P = 0.03\)), and social work (97%, \(P = 0.002\)) consultations (Table 2).

Discharge

Patients were hospitalized for a median time of 6 days (IQR 3–16). Discharge was planned for 249 (77%) patients, premature for 64 (20%), ‘other’ for four (1%), and five (2%) patients died during hospitalization. Patients with a planned discharge had median admission duration of 7 days compared with 3 days for premature discharge. Patients were predominately discharged home (143, 45%), to a shelter or other unstable housing (48, 15%), and to medical inpatient rehab (44, 14%).

In logistic regression analysis, MOUD receipt (OR 3.87, \(P < 0.0001\)), MOUD initiation (OR 4.85, \(P = 0.003\)), and completed addiction consult (including all sites, OR 1.60, \(P = 0.002\); only sites with addiction consultation capacity OR 1.36, \(P = 0.002\)) were significantly associated with higher odds of planned discharge.

Postdischarge parenteral antimicrobial therapy

Of 249 patients with a planned discharge, 177 (71%) completed parenteral antimicrobials by discharge, 50 (20%) were continued on parenteral antimicrobials as an outpatient, 20 (8%) were switched to oral or long-acting injectable therapy, and one (0.4%) left without a plan for postdischarge antimicrobial therapy.

Of 64 patients with a premature discharge, six (9%) completed parenteral antimicrobials by discharge, 12
(19%) were switched to oral or long-acting injectable therapy, and 46 (72%) left without a plan for postdischarge antimicrobial therapy.

Of 129 (40%) patients who had not completed parenteral antimicrobial therapy by discharge, patients who experienced premature discharge were significantly more likely to leave without a plan for postdischarge antimicrobial therapy compared with those with a planned discharge (P < 0.0001).

**Medication for opioid use disorder on discharge**

Of 317 patients who survived to discharge, 129 (40%) had MOUD on their discharge prescription list (Fig. 3a), including 79% of patients on baseline MOUD (Fig. 3b), and 24% of patients not on baseline MOUD (Fig. 3c). In

<table>
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<th>Table 1. Baseline demographics and admission information.</th>
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*Out of patients with completed urine drug screen.
logistic regression analysis of all sites, MOUD receipt (OR 129.7, \( P < 0.0001 \)), and MOUD initiation (OR 345.2, \( P < 0.0001 \)) were significantly associated with higher odds of MOUD prescription on discharge. For the three sites with available addiction consultation, MOUD on discharge was not significantly associated with completed addiction consult (OR ¼ 2.78, \( P = 0.16 \)).

### Linkage to outpatient medication for opioid use disorder

Twenty-seven (9%) patients attended at least one MOUD visit within the health system in the year following admission (Fig. 3a), including 11% on baseline MOUD (Fig. 3b) and 7% not on baseline MOUD (Fig. 3c). Of patients for whom outpatient MOUD follow-up was recommended in the discharge summary, visit attendance was significantly more likely when an appointment was scheduled at the time of discharge compared with when outpatient contact information was given or follow-up was only advised (32 vs. 3%, \( P = 0.0001 \)). In logistic regression analysis, linkage to outpatient MOUD was significantly associated with MOUD receipt (OR 1.25; \( P < 0.0001 \)) and completed addiction consult (OR 1.82; \( P = 0.01 \)).

### Emergency department visits after sentinel admission

In the year following admission, 163 (51%) patients had an emergency department visit without admission within the hospital system, including 57 (18%) patients who had an emergency department visit within 30 days of discharge. People with an emergency department visit...
had a median of two visits (IQR 1–4; range 1–87) within a year, and a median of one emergency department visit (IQR 0–2; range 0–24) related to OUD. In total, there were 833 emergency department visits without admission in the year following sentinel admission, including 109 emergency department visits within 30 days (Supplemental Figure 1, http://links.lww.com/QAD/C911).

Readmissions
One hundred and fifty-nine patients (50%) had at least one readmission in the year following sentinel visit, with a median of two (IQR 1–3; range 1–15) readmissions, including 52 (16%) patients with readmissions within 30 days. Median time to first readmission was 64 days (IQR 17–146). Of people with any readmission, 75% had at least one readmission related to OUD, and 73% had at least one readmission related to infection. In total, there were 398 readmissions in the year following sentinel admission, including 58 readmissions within 30 days (Supplemental Fig. 1, http://links.lww.com/QAD/C911).

In logistic regression analysis, readmission within 30 days, readmission within 1 year, and time to readmission or death were not significantly associated with MOUD receipt ($P = 0.64$, 0.68, 0.72, respectively), MOUD initiation ($P = 0.21$, 0.07, 0.36, respectively), or completed addiction consult (including all sites $P = 0.34$, 0.20, 0.70; excluding site without addiction consultation $P = 0.72$, 0.46, 0.44, respectively).

Compared with stably housed individuals, being unstably housed was significantly associated with higher odds of readmission within 30 days and 1 year, and higher rates of readmission (all $P < 0.05$).

Mortality
Within the 1-year follow-up period, 15 (5%) patients (median age 32, IQR 27–45) were known to have died. Five patients died during sentinel hospitalization, and 10 died in the year following admission. Median time to death was 138 days (IQR 21.5–243.5) and was OUD-related in 7 (47%) patients.

Discussion
In this multisite study of hospitalized people with OUD with injection-related infections, we found dramatic undertreatment of OUD across the care continuum. During hospitalization, less than half of patients ever received MOUD, with initiation occurring in less than a third of eligible patients. These suboptimal rates of MOUD initiation are consistent with previous studies, and reinforce the systematic undertreatment of OUD in patients hospitalized with infectious complications of
Fig. 3. Medication for opioid use disorder continuum showing percentage of patients who received medication for opioid use disorder during hospitalization, had medication for opioid use disorder on discharge medication list, and linked to medication for opioid use disorder within a year of discharge for all patients (a), patients on medication for opioid use disorder prior to admission (b), and patients not on medication for opioid use disorder prior to admission (c).
injecting opioids [11,12]. The fact that the majority of patients were not receiving standard-of-care addiction treatment during hospitalization or on discharge reinforces a care gap for substance using populations, and indicates an unsettling lack of prioritization of OUD care during inpatient admission to outpatient linkage to care. Although short-term outcomes seem to be impacted by care provided in the hospital, long-term outcomes likely require both linkage to and retention in community-based treatment after discharge. While one-year linkage to MOUD within the system was associated with inpatient MOUD and addiction consultation, rates of linkage remained low (9%) but increased significantly when an appointment was scheduled at the time of discharge. These data underscore that to maximize MOUD linkage, patients likely require postdischarge care coordination, and must receive timely outpatient addiction care. Previous research supports that patient navigation may be a key intervention to improve continuity of care and reduce readmission [28]. Furthermore, in a study of discharged patients recommended linkage to outpatient buprenorphine, patients with a wait time of 0–1 day for an MOUD appointment had 2.6 times higher odds of arriving to their appointment compared with two or more days of wait time [29]. Notably, housing instability was associated with higher odds of readmission, and higher rates of readmission. This underscores the complex psychosocial needs of this population, and highlights how addressing psychosocial needs in parallel to addiction may be critical to prevent readmissions and improve overall health of PWID [30].

The CHOICE investigation also found a 50% readmission rate within one year of hospitalization, regardless of inpatient MOUD provision or addiction consultation. Although short-term outcomes seem to be impacted by care provided in the hospital, long-term outcomes likely require both linkage to and retention in community-based treatment after discharge. While one-year linkage to MOUD within the system was associated with inpatient MOUD and addiction consultation, rates of linkage remained low (9%) but increased significantly when an appointment was scheduled at the time of discharge. These data underscore that to maximize MOUD linkage, patients likely require postdischarge care coordination, and must receive timely outpatient addiction care. Previous research supports that patient navigation may be a key intervention to improve continuity of care and reduce readmission [28]. Furthermore, in a study of discharged patients recommended linkage to outpatient buprenorphine, patients with a wait time of 0–1 day for an MOUD appointment had 2.6 times higher odds of arriving to their appointment compared with two or more days of wait time [29]. Notably, housing instability was associated with higher odds of readmission, and higher rates of readmission. This underscores the complex psychosocial needs of this population, and highlights how addressing psychosocial needs in parallel to addiction may be critical to prevent readmissions and improve overall health of PWID [30].

This study had several limitations. This was a retrospective study, so causality between interventions and outcomes could not be determined. Included patients were identified first by ICD codes, with known limitations in the sensitivity of this strategy [31–33]. Further, we only had access to records from the four included healthcare systems. Therefore, postdischarge data for readmission rates, linkage to MOUD, and death are likely incomplete and underestimated. This may be especially true in regards to linkage to MOUD, where care is often largely available in nonacademic community settings and opioid treatment programs. Lastly, these were all academic medical systems, therefore, results may not be generalizable to all settings.

In conclusion, in this evaluation of the continuum of care for patients hospitalized with infectious complications of injecting opioids at four major academic medical centers, there was dramatic undertreatment with MOUD from inpatient admission to outpatient linkage to care. Furthermore, we found underutilization of addiction consultation services, and high rates of premature discharge and readmission. Although inpatient addiction interventions were associated with improved hospital-based outcomes and postdischarge MOUD linkage, the question of how to reduce readmission in these patients remains unanswered, and requires prospective, interventional, and longitudinal investigation.
The CHOICE data suggest that engagement in addiction care through addiction consultation, provision of MOUD, and linkage to care is a critical first step in improving the continuum of care for hospitalized individuals with OUD, requiring a paradigm shift away from learned indifference towards evidence-based practice.

Acknowledgements

We acknowledge Robert Eisinger, PhD, Emade Ebah MPH, Rachel Silk RN MPH, Donna Williams, and Kaylie Burgan, MA.

Funding Support: NIAID, OAR, Emory CFAR, DC CFAR, UAB CFAR. This project was funded by the National Institute of Allergy and Infectious Diseases and the manuscript resulted in part from research supported by the Office of AIDS Research (HHSN269201400012C), Center for AIDS Research, Emory University (P30AI050409), District of Columbia Center for AIDS Research (P30AI117970), and Center for AIDS Research, University of Alabama, Birmingham (P30AI027767). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Conflicts of interest

E.S.R. reports investigator-initiated grants paid to the institution from Gilead and Merck, and investigator-initiated grants paid to the institution from Merck and received grants from Gilead and Arbutus. G.A.B reports investigator-initiated grants paid to the institution from Gilead.

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