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## Impact of an addiction medicine consult service on patients admitted to the hospital with injection drug use-associated infective endocarditis

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# **Impact of an addiction medicine consult service on patients admitted to the hospital with injection drug use-associated infective endocarditis**

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## **ABSTRACT**

**Background:** The addition of an addiction medicine consult service has been shown to improve mortality and decrease hospital costs but its impact on the proportion of patients discharged against medical advice (DAMA) and in-hospital initiation of medication for opioid use disorder (MOUD) has not been examined.

**Methods:** A retrospective before-after cohort study was performed at an urban, academic medical center between January 1, 2015 and November 1, 2019. We included adult patients with infective endocarditis and injection drug use determined by admitting diagnosis ICD-9 or ICD-10 codes or documentation within the history section of electronic health record . Our institution implemented a formal addiction medicine consult service on July 1, 2018. We determined the proportion of patients DAMA and the proportion of patients started on MOUD among patients in the pre-intervention (i.e. hospitalized before July 1, 2018) and intervention (i.e. hospitalized July 1, 2018 or after) groups.

**Results:** A total of 171 hospitalized patients with injection drug use-associated infective endocarditis were included with 119 patients in the pre-intervention group and 52 patients in the intervention group. There was no statistically significant difference in patients DAMA [19% vs 15%, absolute risk difference 4.6% (95% confidence interval -8.6% to 17.7%)] between the intervention and pre-intervention groups.

However, there was an increase in the proportion of inpatient MOUD initiation in the intervention group

compared to the pre-intervention group [56% vs 21%, absolute risk difference 35% (95% confidence interval 19% to 50%)].

Conclusions: The initiation of an addiction medicine consult service was associated with a higher proportion of MOUD initiation but there was no statistically significant association with the proportion of patients DAMA.

**Keywords:** addiction medicine consult service, infective endocarditis, injection drug use

## INTRODUCTION

### Background and rationale

Injection drug use predisposes patients to dangerous complications beyond overdose, including skin and soft tissue infections, bone and joint infections, endocarditis, as well as transmissible diseases such as viral hepatitis and human immunodeficiency virus. Such complications lead to emergency department utilization and frequently, subsequent hospital admission<sup>1</sup>. Research has shown that the number of hospitalizations related to opioid use with associated infections nearly doubled (3,421 to 6,535) and total charges more than tripled (\$191 million to \$701 million) from 2002 to 2012 in the United States<sup>2</sup>. In North Carolina, it was found that the incidence of drug dependence combined with endocarditis specifically increased more than twelvefold (0.2 to 2.7 per 100,000 persons per year) from 2010 to 2015 with corresponding hospital costs increasing eighteen-fold (\$1.1 million to \$22.2 million) during that time frame<sup>3</sup>. Unfortunately, the proportion of patients discharged against medical advice (DAMA) is also rising (11.7% to 21.0% from 2010 to 2015) among patients with injection drug use-associated infectious endocarditis across the country<sup>4</sup>. Recent drug use has been shown to be a risk factor for patients to be DAMA and in-hospital methadone use has been shown to be protective against patients who are DAMA<sup>5</sup>. Addiction medicine consult services and primary addiction medicine admitting services are becoming more prevalent as hospitalization rates for substance use disorders and associated complications continue to rise. With this service, patients with recent substance use are linked with addiction medicine specialists as part of their inpatient care team. Addiction medicine consultants treat withdrawal and intoxication, perform motivational interviewing, initiate medication for opioid use disorder (MOUD) as well as medications for other use disorders, and facilitate outpatient follow-up. Most importantly, consultants create therapeutic partnerships with the patients with substance use disorder who often fear stigma from the medical community<sup>6</sup>. Recent studies show that an addiction consult service can effectively link hospitalized patients with substance use disorders to outpatient addiction treatment in the form of MOUD such as buprenorphine, methadone, or naltrexone<sup>7</sup>. Investigators have also found that admitting patients to specialty inpatient primary services improves mortality as well as decreases cost when compared to being

admitted to a general internal medicine hospitalist service<sup>8,9</sup>. However, to date, there are few studies that investigate the impact of an inpatient addiction medicine consult service on hospital outcomes such as the proportion of patients DAMA and MOUD initiation.

## **Objectives**

The objective of this study was to test the impact of implementing an inpatient addiction medicine consult service on the proportion of (1) patients DAMA and (2) in-hospital MOUD initiation among hospitalized patients with injection drug use-associated infective endocarditis. We hypothesized that patients receiving a consult from a specialized addiction medicine service would have a lower risk of being DAMA and a higher likelihood of in-hospital MOUD initiation. Our rationale for this hypothesis was that an addiction consult service would prescribe more MOUD, thereby decreasing opioid withdrawal which is a common reason for patients leaving prior to treatment completion.

## **METHODS**

### **Study design and setting**

This is a retrospective, before-after cohort study of patients with recent injection drug use hospitalized for infective endocarditis at an urban, academic medical center in the United States. The Institutional Review Board at our institution approved this study with waiver of informed consent. The results are reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement<sup>10</sup>.

### **Participants**

We queried our electronic medical record EPIC<sup>TM</sup> (EPIC Systems Corporation, Verona, WI) to identify patients admitted to our facility between January 1, 2015 (when our hospital first started staffing addiction medicine consultations) and November 1, 2019 who met the following inclusion criteria: (1) age greater than or equal to 18 years old and (2) admitting diagnosis ICD-9 and ICD-10 codes related to infective endocarditis and injection drug use or intravenous drug use listed in the medical history section of the electronic health record (EHR). Exclusion criteria included documented lack of capacity to refuse medical treatment (i.e. lack of capacity to be DAMA). There was no formal advertising nor encouragement from hospital leadership for primary teams to consult the addiction medicine service. The consult service grew organically over time.

## **Variables**

We recorded patient demographics, medical comorbidities, substance use history, hospitalization level of care, hospital length of stay, whether patients were DAMA, in-hospital mortality, whether opioids were administered while hospitalized, whether a valve replacement was offered or performed, whether an addiction medicine consult was placed and staffed, whether MOUD was administered in the hospital, and if so, what type of MOUD was initiated.

## **Data sources and measurement**

Two investigators reviewed the EHR for each subject and abstracted the data. Both abstractors had previous experience using EPIC and underwent a formal training session including performing joint data extraction on a set of practice medical records to ensure uniform handling of data. A standardized data extraction form and predefined definition of variables were used for all data collection. The abstractors held periodic meetings to review coding rules and to monitor performance. We calculated an inter-observer agreement using the kappa statistic between the two abstractors based on a 10% sample of cases selected at random<sup>11</sup>. Disagreement was reconciled by a third investigator who abstracted the same sample data. Before continuing data collection, all abstractors came to a consensus on coding rules.

## **Study size**

Assuming (1)  $\alpha = 0.05$ , (2) power = 0.8, and (3) an allocation ratio of two to one patients in the pre-intervention and intervention groups respectively, to detect a 15% difference in patients DAMA between the pre-intervention and intervention groups (20% vs. 5%, respectively) using a two-sided test, a sample of 153 total patients was required (102 in the pre-intervention group and 51 in the intervention group).

## **Intervention**

Our institution has had physicians board certified in addiction medicine since 2015; however, these physicians practiced primarily in the outpatient setting and had limited availability to see inpatient consultations. On July 1, 2018, a new faculty member was hired specifically to staff inpatient consultations marking the establishment of a formal inpatient addiction medicine consult service. During the intervention period, the addiction medicine consult service comprised a rotation of five physicians board certified in addiction medicine from various primary specialties (internal medicine, family medicine, emergency medicine, and psychiatry).

## **Quantitative variables**

The primary outcome was the proportion of patients DAMA among those who survived to hospital discharge. The secondary outcome was the proportion of patients who received inpatient MOUD among those who survived to hospital discharge. Study data were collected and managed using Research Electronic Data Capture (REDCap) tools hosted at Rowan University<sup>12,13</sup>. “REDCap (Nashville, TN) is a secure, web-based application designed to support data capture for research studies. It provides: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.” Data was then exported into Stata/SE 16.1 for Mac, StataCorp LP (College Station, TX, USA) for analysis.

## **Statistical methods**

For the purposes of analysis, patients were divided into two groups: (1) pre-intervention group (i.e. hospitalized prior to the initiation of the formal addiction medicine consult service on July 1, 2018) and (2) intervention group (i.e. hospitalized after implementation of the consult service). We compared the two groups with respect to baseline demographics, comorbidities, and prognostic factors using Fisher’s exact test for categorical data and student’s t-test or Mann-Whitney test as appropriate for continuous data.

We compared the proportion of patients DAMA and the proportion of patients who had MOUD initiated between the two groups by calculating the absolute risk difference with 95% confidence intervals (CI). We also compared the proportion of patients DAMA who had MOUD initiated in hospital compared to those who did not by calculating the absolute risk difference with 95% CI. Hospital length of stay was compared between the two groups by calculating the mean difference with 95% CI.

## **RESULTS**

### **Participants**

A total of 183 patients were screened for inclusion. Twelve patients were excluded because their medical records lacked documentation of recent injection drug use or lacked a clear diagnosis of infective endocarditis. Ultimately, 171 patients were included in the final cohort. Of those, 119 patients presented in the pre-intervention period and 52 patients presented in the intervention period.

## **Descriptive data**

Baseline characteristics were similar between the two groups except for a greater proportion of White patients in the intervention group compared to the pre-intervention group (88% vs 74%,  $p = 0.050$ ) (Table 1). A significantly higher proportion of patients in the intervention group received a formal addiction medicine consultation compared to the pre-intervention group (60% vs. 13%, respectively), absolute risk difference of 46% (95% CI 31% to 61%).

Severity of illness was similar between the two groups with 43% requiring intensive care unit admission in the pre-intervention group versus 40% requiring intensive care unit admission in the intervention group. Overall mortality was 12% (21/171) and similar between the two groups: 10% (5/52) in the intervention group and 13% (16/119) in the pre-intervention group with an absolute risk difference of -3.8% (95% CI -13.9% to 6.3%).

Inter-observer agreement among data abstractors was acceptable for all variables tested ( $\kappa = 0.68$ ).

## **Outcome data and main results**

Overall, 16% (24/150) of those who survived to hospital discharge had the primary outcome of being DAMA. We did not find a statistically significant difference in the primary outcome between the intervention and pre-intervention groups (19% vs. 15%, respectively), absolute risk difference of 4.6% (95% CI -8.6% to 17.7%) (Table 2).

The proportion of patients with MOUD initiated in-hospital was higher in the intervention group compared to the pre-intervention group (56% vs 21%, respectively), absolute risk difference of 35% (95% CI 19% to 50%).

The overall median [interquartile range (IQR)] length of stay among survivors was 15 (9 - 32) days and similar between the intervention and pre-intervention groups [16 (9 - 32) vs. 15 (9 - 32) days, respectively], mean difference of 0.5 (95% CI -6 to 7) days.

## **Analysis of subgroups**

Of all patients who were initiated on MOUD ( $n=52$ , across both time periods), 21% (11/52) were DAMA. In comparison, of all patients who were not initiated on MOUD ( $n=98$ , across both time periods), only 13% (13/98) were DAMA, absolute risk difference of 7.8% (95% CI -5.0% to 20.9%). Among all patients DAMA ( $n=24$ , across both time periods), 21% (5/24) were initiated on methadone, 25% (6/24) were initiated on buprenorphine, and 54% (13/24) did not have initiation of MOUD while in the hospital. Of all patients seen by the addiction medicine consult service, 24% were DAMA and of all patients not



seen by the addiction medicine consult service, 12% were DAMA [24% vs 12%, absolute risk difference 12% (95% confidence interval -2% to 26%)]. Of all patients in the intervention group (n=52) who received addiction medicine consultations (n=31), 81% (25/31) initiated MOUD compared to 19% (4/21) of patients who did not receive addiction medicine consultations (n=21).

## **DISCUSSION**

### **Key results**

In this study, we compared the proportion of patients who were DAMA and the proportion of patients initiated on MOUD among patients hospitalized for infective endocarditis with recent injection drug use before and after the initiation of an addiction medicine consult service. In this cohort of 171 patients, we found that during the intervention period, there was an increased proportion of patients with a formal addiction medicine consultation and MOUD initiation in-hospital compared to the pre-intervention group. However, there was no statistically significant difference in the proportion of patients who were DAMA between the two groups.

### **Interpretation**

Although the intervention group had a significantly higher proportion of addiction medicine consultations ordered compared to the pre-intervention group (60% vs 13%), this still meant that providers did not order consultations for 40% of patients with infective endocarditis and injection drug use after initiation of the formal consult service. In a separate study at a large tertiary care center that examined a similar patient population, only 55% of patients had addiction medicine mentioned in their discharge planning and only 7% had a plan for MOUD initiation<sup>14</sup>. These statistics suggest that there is inadequate linkage to addiction care for patients with substance use disorders even at institutions with dedicated addiction medicine consult services. It is possible that at our institution, primary providers did not order addiction medicine consultations because they were not aware of the presence of the consult service, they felt comfortable treating the substance use disorder without the assistance of an addiction medicine specialist, or the patient declined the consult.

The increase in initiation of MOUD during the intervention period (56% vs 21%) could be attributed to the establishment of a specialty service staffed by addiction-trained faculty who are not only better at recognizing the indications for MOUD but are also more comfortable initiating patients on methadone and buprenorphine in the hospital setting and less fearful of precipitating withdrawal. Providers (physicians and mid-level practitioners) with a valid DEA license must apply for an X-waiver in order to prescribe

buprenorphine in the outpatient setting. The only situation in which non-X-waivered providers can provide patients with buprenorphine is for hospitalized patients as long as buprenorphine is on the hospital's formulary<sup>15</sup>. All the physicians who staffed our addiction medicine consult service were X-waivered to prescribe buprenorphine, but it is not known whether all practitioners on the primary medical teams had this delineation. Research has shown that physicians with this additional certification have more positive attitudes toward prescribing buprenorphine compared to physicians who are not X-waivered<sup>16</sup>.

Of the patients who were initiated on MOUD, there was still a significant proportion of them (21%) who were DAMA compared to only 13% of patients DAMA not initiated on MOUD. A similar pattern was observed for patients seen by the consultation service (24% DAMA) compared to patients not seen by the consultation service (12% DAMA). This finding may suggest that addiction medicine consultations and MOUD were disproportionately ordered for the more psychosocially complex patients who were already at higher risk of being DAMA. Factors other than opioid withdrawal may have contributed to these patients being DAMA such as discrimination by hospital staff and restricted hospital policies<sup>17</sup>, in which case interventions beyond the initiation of an addiction medicine consult service may have been necessary to see a reduction in the proportion of patients DAMA.

### **Limitations and generalizability**

We acknowledge that this study has several important limitations. First, this was a single center, retrospective study. Given the retrospective design, patients that met our inclusion criteria in either group may have been missed due to improper or inadequate diagnostic code designations. However, since we sought to identify a focused patient population (specifically, patients with infective endocarditis), it is unlikely that patients were overlooked secondary to missing diagnostic codes. Additionally, as our addiction medicine consult service was relatively new, there was just over one year of data available in the intervention group and hence proportionally less patients in comparison to approximately three years of data analyzed in the pre-intervention group. Similarly, given the study design, we can only comment on associations between the initiation of the consult service and patient outcomes and cannot infer causation. Second, both groups had a predominance of White participants which limits the generalizability of our findings to individuals of other races and ethnicities and raises additional questions from a cultural perspective given a much more diverse demographic of the surrounding community. According to a recent article, an underrepresentation of minority populations in research studies could be due to distrust of the medical system, especially with regards to the African American population and with sensitive medical treatments like addiction care<sup>18</sup>. Third, we did not assess the reasons for patients with DAMA. While studies have found that treating (or preventing) opioid withdrawal is associated with improved clinical

outcomes for patients<sup>19</sup>, we did not find an association between increased proportion of MOUD initiation and decreased proportion of patients DAMA.

At our institution, we did not identify a statistically significant association between the initiation of an addiction medicine service and the proportion of patients DAMA, though the observed confidence intervals do not rule out such a relationship. At other institutions, addiction consult services have been shown to improve other clinical outcomes for patients with substance use disorders such as increased medical insurance coverage, decreased homelessness, and decreased addiction severity<sup>6</sup>. For opioid use disorder specifically, opioid agonist medications are best practice for both withdrawal treatment and maintenance therapy. Patients admitted with infectious complications of injection drug use are particularly vulnerable to relapse; hence, the opportune setting to initiate MOUD is during the inpatient encounter. At our institution, the initiation of an addiction medicine consult service was associated with increased engagement in MOUD. Therefore, implementing an addiction medicine consult service may be one avenue to increase patients' access to highly specialized addiction care and improve the overall treatment of individuals with substance use disorders.

### **Future directions**

Our study represents an initial analysis of the impact of an addiction medicine consult service at a single institution. Future research should expand to include a larger sample size with addition of data from neighboring health systems and patients with other infectious complications of injection drug use which will more completely assess an association between rate of DAMA with rate of MOUD initiation, readmission risk, and mortality. An additional facet would be to perform a cost savings analysis.

### **CONCLUSIONS**

The initiation of an addiction medicine consult service was associated with a higher proportion of MOUD initiation in hospitalized patients with injection drug use-associated infective endocarditis but did not significantly correlate with differences in the proportion of patients DAMA. These results suggest that untreated withdrawal is not solely responsible for patients leaving prior to treatment completion. Further investigation into other risk factors for patients being DAMA and interventions to reduce these risk factors is warranted.

[Table 1 about here.]

SD, standard deviation; IQR, interquartile range

[Table 2 about here.]

ICU, intensive care unit; MOUD, medications for opioid use disorder; IQR, interquartile range

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**Table 1** Baseline patient characteristics

Variables	All Subjects n = 171	Pre-consult service period n = 119	Consult service period n = 52	p - value
Age [years (SD)]	37 (10)	37 (10)	38 (10)	0.80
Female [n (%)]	77 (45)	51 (43)	26 (50)	0.41
Race [n (%)]				
White/Caucasian	134 (78)	88 (74)	46 (88)	
Black/African American	29 (17)	23 (19)	6 (12)	0.05
Other	8 (5)	8 (7)	0	
Hispanic Ethnicity [n (%)]	21 (12)	18 (15)	3 (6)	0.19
Pre-existing comorbidities [n (%)]				
Diabetes	9 (5)	9 (8)	0	0.06
Coronary artery disease	0	0	0	
Hypertension	30 (18)	18 (15)	12 (23)	0.27
Malignancy	3 (2)	2 (2)	2 (2)	> 0.99
Renal insufficiency	8 (5)	5 (4)	3 (6)	0.70
Pulmonary disease	22 (13)	14 (12)	8 (15)	0.62
Cerebral vascular disease	6 (4)	4 (3)	2 (4)	> 0.99
Congestive heart failure	3 (2)	3 (3)	0	0.55
Charlson comorbidity score median [IQR]	0 (0-1)	0 (0-1)	0 (0-1)	0.25
Domiciled [n (%)]	134 (78)	95 (80)	39 (75)	0.55

**Table 2** Clinical outcomes pre- and post-addiction consult service initiation

Variables	All Subjects n =	Pre-consult service period	Consult service period	p - value
	171	n = 119	n = 52	
Admission to ICU	72 (42)	51 (43)	21 (40)	0.87
Addiction consult ordered	47 (27)	16 (13)	31 (60)	<0.001
MOUD	54 (32)	25 (21)	29 (56)	<0.001
Methadone	27 (16)	17 (14)	10 (19)	0.50
Dose (mg) [median (IQR)]	40 (30-80)	30 (25-80)	40 (30-70)	0.52
Buprenorphine	27 (16)	8 (7)	19 (37)	<0.001
Dose (mg) [median (IQR)]	10 (8-16)	13 (8-16)	8 (8-16)	0.85