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MAJOR ARTICLE

Integrated Infectious Disease and Substance Use Disorder Care for the Treatment of Injection Drug Use–Associated Infections: A Prospective Cohort Study With Historical Control

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Background. To address the infectious disease (ID) and substance use disorder (SUD) syndemic, we developed an integrated ID/SUD clinical team rooted in harm reduction at a county hospital in Miami, Florida. The Severe Injection-Related Infection (SIRI) team treats people who inject drugs (PWID) and provides medical care, SUD treatment, and patient navigation during hospitalization and after hospital discharge. We assessed the impact of the SIRI team on ID and SUD treatment and healthcare utilization outcomes.

Methods. We prospectively collected data on patients seen by the SIRI team. A diagnostic code algorithm confirmed by chart review was used to identify a historical control group of patients with SIRI hospitalizations in the year preceding implementation of the SIRI team. The primary outcome was death or readmission within 90 days post–hospital discharge. Secondary outcomes included initiation of medications for opioid use disorder (MOUD) and antibiotic course completion.

Results. There were 129 patients included in the study: 59 in the SIRI team intervention and 70 in the pre-SIRI team control group. SIRI team patients had a 45% risk reduction (aRR, 0.55 [95% confidence interval CI, .32–.95]; 24% vs 44%) of being readmitted in 90 days or dying compared to pre-SIRI historical controls. SIRI team patients were more likely to initiate MOUD in the hospital (93% vs 33%, $P < .01$), complete antibiotic treatment (90% vs 60%, $P < .01$), and less likely to have patient-directed discharge (17% vs 37%, $P = .02$).

Conclusions. An integrated ID/SUD team was associated with improvements in healthcare utilization, MOUD initiation, and antibiotic completion for PWID with infections.

Keywords. buprenorphine; injection drug use; injection-related infection; opioid use disorder; substance use disorder.

Hospitalizations for injection drug use (IDU)–associated infectious diseases have been increasing in the wake of the ongoing drug overdose crisis [1, 2]. Severe injection-related infections (SIRIs) requiring hospitalization include skin and soft tissue infections (SSTIs), endocarditis, bloodstream infections, and osteoarticular infections, among others. Invasive bacterial and fungal infections among people who inject drugs (PWID) are both a direct cause of mortality as well as a marker for future harms, including overdose, human immunodeficiency virus (HIV) infection, and hepatitis C virus (HCV) infection [3–5]. SIRI hospitalizations among PWID are characterized by prolonged lengths of stay, high healthcare costs, and high rates of patient-directed discharge (PDD) (also known as "against medical advice") [6–8]. PWID hospitalized for SIRI describe untreated withdrawal symptoms and pervasive stigma from healthcare providers based on their substance use [9, 10].

Several efforts to help mitigate the gaps in care for PWID hospitalized with infections have been evaluated. Multidisciplinary approaches that integrate infectious disease (ID) and addiction care in the hospital have shown promise in addressing many of the barriers to successful individual and health system outcomes [11]. Existing models include ID specialists, addiction medicine specialists, psychiatrists, and surgeons and may incorporate pharmacotherapy, behavioral treatments, harm reduction, and linkage

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to postdischarge follow-up [12–15]. Previous research has demonstrated that integration of evidence-based addiction treatment—such as medications for opioid use disorder (MOUD)—with ID care is associated with lower rates of PDD [16, 17] and hospital readmission [12, 18], reduced substance use [19], and higher rates of antimicrobial therapy completion [16, 20]. There is a critical need to understand how best to implement these evidence-based interventions into clinical practice.

To address the current ID and SUD syndemic and build on existing models, we developed an integrated ID/SUD clinical team intervention rooted in harm reduction. The SIRI team meets the needs of PWID hospitalized with acute bacterial or fungal infections by focusing on pragmatic antimicrobial plans, improving comfort, and helping treat SUD for those who are receptive. The team uses a harm reduction approach [21], provides intensive care coordination, focuses on low-barrier access to MOUD, and utilizes individualized ID treatment approaches, such as oral antibiotics and long-acting lipoglycopeptide antibiotics. By harnessing connections with the local syringe services program (SSP), residential addiction treatment programs, and housing services, in addition to clinic and telemedicine capabilities, the team provides ID and SUD care tailored to each individual's needs. This study sought to evaluate the impact of the SIRI team intervention on healthcare utilization, ID, and SUD outcomes.

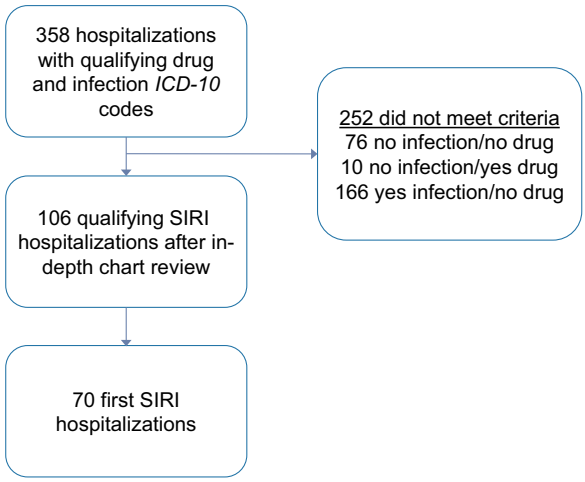

Figure 1. Flow diagram of construction of retrospective control cohort. Diagram demonstrating results of diagnostic code search algorithm to identify severe injection-related infection (SIRI) hospitalizations in the control period (March 2019–February 2020). Hospitalizations were identified that contained a diagnostic code for drug use and for infection. Charts were individually reviewed to determine if the hospitalization was for a SIRI. For the 252 excluded cases, despite the diagnostic codes, no evidence of a valid infection, probable injection drug use, or neither was identified. For individuals with multiple SIRI hospitalizations in the study period, only the first was used. Abbreviations: *ICD-10*, *International Classification of Diseases, Tenth Revision*; SIRI, severe injection-related infection.

METHODS

Human Subjects

The study was approved by the institutional review board (IRB) of the University of Miami and the clinical trials office of Jackson Memorial Hospital (IRB 20200962). There was a waiver of informed consent for retrospectively collected data. Informed consent was obtained from patients in the hospital or after discharge prior to prospective data collection.

Study Setting and Design

In August 2020, Jackson Memorial Hospital, a 1550 bed safety-net hospital in Miami, Florida, implemented the SIRI team to care for patients hospitalized with IDU-associated bacterial and fungal infections. SIRI team patients were prospectively enrolled into an observational cohort between August 2020 and May 2022 to measure infection cure, substance use, and healthcare utilization outcomes. Data were compared to a retrospectively identified cohort of patients hospitalized at the same hospital with an IDU-associated infection in the year preceding SIRI team implementation (historical controls).

To construct the retrospective pre-SIRI team control cohort, the medical record was queried for hospitalizations of ≥48 hours' duration from March 2019 through February 2020 using *International Classification of Diseases, Tenth Revision* (*ICD-10*) codes for both a substance use diagnosis and an infection diagnosis compatible with IDU. Inclusion was limited to hospital stays of ≥48 hours to increase the likelihood that, had the SIRI team existed at the time, there would have been enough time for them to be consulted. We did not include data between March and August 2020 due to severe care disruptions early in the coronavirus disease 2019 pandemic. Due to previous research suggesting misclassification of *ICD-10*–based algorithms to accurately identify hospitalizations for IDU-associated infection [22, 23], all records were individually reviewed to determine if the patient met SIRI team criteria. Figure 1 presents a flow diagram of how the control cohort was developed. If a patient had multiple hospitalizations for a SIRI within the study period, only the first hospitalization was used.

Data were abstracted from the patient's medical record for both the intervention and control groups. All chart abstractions were reviewed by an additional study team member to confirm fidelity. Patients in the SIRI team group included all first-time SIRI team patients who were diagnosed with an infection. Abstracted data were inputted into a database management software, REDCap, to ensure patient information remained protected [24].

SIRI Team Intervention

The SIRI team intervention targets patients admitted with an acute bacterial or fungal infection and having an indication of IDU in the prior year. IDU is assessed by self-report from

the patient, physical examination with stigmata of injection, or based on the presence of an infection typical of IDU (eg, purulent SSTI) along with diagnosis of opioid use disorder (OUD). The SIRI team is consulted directly by hospitalists, critical care, or surgical services as well as referrals from the general ID consult service. Once consulted, the SIRI team provides both ID and SUD care during the hospital stay and for 90 days after discharge. There is a strong focus on managing pain, withdrawal, and anxiety and serving as a patient advocate during their hospital stay. After discharge, the team follows patients closely into the community with frequent contact, low-barrier communication, ongoing provision of ID/SUD care, and assistance navigating social determinants of health. The team consists of 3 physicians with expertise in ID and addiction medicine, an ID nurse practitioner, and additional assistance from a pain stewardship pharmacist and the affiliated SSP's team of peer counselors and social workers. A detailed description of the SIRI team intervention has been previously reported [25].

Control Condition

Preimplementation of the SIRI team intervention, the standard of care for patients with IDU-associated infections consisted of hospital care by hospitalist teams in consultation from infectious disease, psychiatry, and surgical services. Hospitalists and psychiatrists may or may not have had experience initiating MOUD with others favoring passive referral to posthospital services. The health system has an affiliated outpatient MOUD program housed in their behavioral health hospital to which some patients were passively referred. Posthospital care included discharge with a referral to ID clinic when ID follow-up was warranted.

Data Collection and Measures

Data were abstracted from all parts of the medical record including physician notes, social work notes, laboratory values, microbiology results, medication administration record, and diagnostic imaging. Substance use was identified by physician notes—particularly psychiatry and ID notes, urine drug screening results, and preceding inpatient detoxification program notes. We categorized patients as using an opioid if there was evidence of heroin, illicit fentanyl, or opioid analgesic use within the prior year. Stimulants included the use of cocaine, methamphetamine, amphetamine, and 3,4-methylenedioxy-methamphetamine (MDMA).

Infection diagnoses were obtained from ID clinician notes, when available, and were inclusive of all acute bacterial/fungal infections present. For example, endocarditis from a soft tissue infection was coded as having endocarditis, SSTI, and bacteremia present. We created a category of *severe infection* including *Staphylococcus aureus* bacteremia, endocarditis, osteomyelitis, septic arthritis, fungemia, prosthetic device infection, or septic pulmonary emboli. These were chosen as infections with elevated mortality rate, or which traditionally have been treated with ≥14-day courses of antibiotics. Antibiotic recommendations included recording of the projected length of treatment and the route of therapy at the time of discharge. For OUD treatment, we included administration of any doses of buprenorphine or methadone during hospitalization as MOUD initiation. We also recorded whether buprenorphine was prescribed upon discharge or if explicit plans for follow-up at a methadone clinic were documented. For patients in the SIRI team condition, additional postdischarge data included validated self-report of whether patients were using MOUD or other substances at 90 days as well as their housing status at 90 days.

Outcomes

The primary outcome for this study was hospital readmission to Jackson Memorial Hospital (medical record) or death (medical record and public Miami-Dade County medical examiner database) within 90 days of discharge. For SIRI team patients, death was also assessed by communication with emergency contacts. The readmission outcome was chosen to represent an outcome that is relevant to both health systems (which are penalized for readmissions) and PWID (who often avoid healthcare due to stigma and mistreatment). Mortality was included in the composite to ensure that postdischarge death without readmission was not counted as a positive outcome. Secondary outcomes included readmission and mortality individually, completion of antibiotic course, initiation of MOUD, length of stay, and PDD. Completion of antibiotics was determined from clinical notes. If a patient left under PDD and no antibiotics were prescribed, it was assumed that antibiotics were not completed. If a patient was discharged on antibiotics and had no further documentation, completion was assumed.

Statistical Analyses

Descriptive statistics were stratified by treatment condition to examine imbalances between the SIRI team and control patients. We compared SIRI team intervention and control patients on demographics, substance use, comorbid conditions, type of infection, services received while inpatient (MOUD, antibiotic course), and discharge characteristics using χ^2 and Fisher exact tests for categorical variables and Wilcoxon rank-sum test for continuous variables. Bivariate and multivariable Poisson regression models with robust standard errors were used to directly estimate the risk ratio associated with the SIRI team intervention on 90-day readmission or death (binary outcome), both unadjusted and adjusting for severity of injection-related infection. Robust Poisson regression models have been shown to provide unbiased estimates of risk ratios under model misspecification [26]. Results were reported as unadjusted (RR) or adjusted relative risk ratio (aRR) with corresponding 95% confidence interval (CI). Finally, we compared the readmission-free survival after hospital discharge between

SIRI team and control patients using Kaplan-Meier survival analysis and log-rank test with events censored at 90 days post-discharge. All analyses were performed using SAS 9.4 statistical software (SAS Institute, Cary, North Carolina) and significance level was set at an α of .05.

RESULTS

Overall Sample

The study sample included 129 patients who were hospitalized with SIRIs. Fifty-nine (45.7%) of the sample received the SIRI team intervention and 70 (54.3%) received standard of care. A majority of patients were male (62.0%), almost half were non-Hispanic White (46.5%), and most were experiencing homelessness at the time of hospital admission (68.2%). Nearly all patients used opioids (99.2%) and stimulants (86.8%). HCV seropositivity was 78.3% and HIV infection was present in 23.4%. There were no significant differences between the SIRI team and control group across demographics, comorbidities, and type of injection-related infection, aside from higher rate of SSTI among controls and more vertebral osteomyelitis among SIRI team patients (Table 1).

Hospitalization Characteristics

Compared to the control condition, SIRI team patients were more likely to receive any type of MOUD during the hospital stay (93.2% vs 32.9%, $P < .01$), be prescribed MOUD upon discharge (98.3% vs 13.2%, $P < .01$), and be provided naloxone (98.3% vs 0%, $P < .01$) (Table 2). All MOUD was methadone or buprenorphine; no patients received extended-release naltrexone. For patients still requiring antibiotics at the time of discharge, SIRI patients were more likely to have been provided oral antibiotics (92.5% vs 55.2%, $P < .01$) whereas 36% in the control group who had indication for ongoing antibiotics left the hospital under PDD and were given none. Oral antibiotics were utilized by 84.4% of SIRI team patients with severe infections. SIRI team patients were less likely to have PDD (17.0% vs 37.1%, $P = .02$). SIRI team patients had longer lengths of stay overall (median, 12 vs 7.5 days, $P < .01$); however, when limiting the analysis to those who did not leave as a PDD, there was no significant difference in length of stay (median, 13 vs 10 days, $P = .12$). There was significant difference in discharge location, with SIRI team patients less likely to discharge to the street (25.9% vs 40.6%) and more likely to discharge to residential addiction treatment (27.6% vs 10.1%).

Posthospitalization Outcomes

The rate of death or hospital readmission within 90 days of discharge was 24.1% among SIRI team patients and 43.5% in the controls. In the multivariable Poisson regression model (Table 3), after adjusting for severity of infection, SIRI team patients had a 45% risk reduction (aRR, 0.55 [95% CI, .32–.95]) of being readmitted or dying in 90 days and a 57% risk reduction (aRR, 0.43 [95% CI, .22–.81]) of being readmitted to the hospital in 90 days compared to the control condition. In addition, SIRI team patients were significantly more likely to have completed their course of antibiotics (aRR, 1.47 [95% CI, 1.19–1.82]). Figure 2 shows the Kaplan-Meier survival curve for readmission-free survival in SIRI team patients and control patients, with patients who received the SIRI team intervention

Table 1. Characteristics of Patients Hospitalized With Severe Injection-Related Infection (SIRI), Stratified by SIRI Team and Control Conditions (n = 129)

Characteristics	Total (N = 129)	SIRI Team (n = 59)	Control (n = 70)	*P* Value
Age, y, median (IQR)	40 (32–49)	41 (32–50)	38 (33–49)	.60
Female sex	49 (38.0)	24 (40.7)	25 (35.7)	.56
Race/ethnicity				.57
Non-Hispanic White	60 (46.5)	29 (49.2)	31 (44.3)	
Non-Hispanic Black	17 (13.2)	9 (15.3)	8 (11.4)	
Hispanic	52 (40.3)	21 (35.6)	31 (44.3)	
Uninsured at admission	69 (53.5)	27 (45.8)	42 (60.0)	.11
Opioids used	128 (99.2)	59 (100.0)	69 (98.6)	.36
Stimulants used[a]	112 (86.8)	50 (84.8)	62 (88.6)	.52
HIV	30 (23.4)	10 (17.0)	20 (28.6)	.13
Hepatitis C[b]	101 (78.3)	47 (79.7)	54 (77.1)	.73
MOUD on admission	12 (9.3)	3 (5.1)	9 (12.9)	.13
Experiencing homelessness	88 (68.2)	42 (71.2)	46 (65.7)	.51
Infections present				
Skin and soft tissue	66 (51.2)	24 (40.7)	42 (60.0)	.03
Skin and soft tissue only[c]	35 (27.1)	13 (22.0)	22 (31.4)	.23
Endocarditis	13 (10.1)	8 (13.6)	5 (7.1)	.23
Bloodstream infection	36 (27.9)	16 (27.1)	20 (28.6)	.85
Osteomyelitis	31 (24.0)	18 (30.5)	13 (18.6)	.11
Nonvertebral	15 (11.6)	7 (11.9)	8 (11.4)	.94
Vertebral	16 (12.4)	11 (18.6)	5 (7.1)	.05
Septic arthritis	14 (10.9)	6 (10.2)	8 (11.4)	.82
Other infection	13 (10.1)	6 (10.2)	7 (10.0)	.92
Severe infection[d]	62 (48.0)	33 (55.9)	29 (41.4)	.10
Organism				
Staphylococcus aureus	55 (42.6)	28 (47.5)	27 (38.6)	
MRSA	36 (27.9)	20 (33.9)	16 (22.9)	
MSSA	19 (14.7)	8 (13.6)	11 (15.7)	
Streptococci	22 (17.1)	11 (18.6)	11 (15.7)	
Gram-negative bacilli	14 (10.9)	7 (11.9)	7 (10.0)	
None identified or cultures not performed	43 (33.3)	17 (28.8)	26 (37.1)	

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: HIV, human immunodeficiency virus; IQR, interquartile range; MOUD, medication for opioid use disorder; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; SIRI, severe injection-related infection.

[a]Included use of cocaine (crack or powder), amphetamine, methamphetamine, and 3,4-methylenedioxy-methamphetamine.

[b]Hepatitis C virus antibody positive.

[c]Indicates patients with skin and soft tissue infection only, and no other SIRI diagnosis.

[d]Severe infection includes *S aureus* bacteremia, endocarditis, osteomyelitis, septic arthritis, fungemia, prosthetic device infection, septic pulmonary emboli.

Table 2. Index Hospitalization Characteristics of Patients With Severe Injection-Related Infection (SIRI) in the SIRI Team and Control Conditions

Characteristics	SIRI Team (n = 59)	Control (n = 70)	*P* Value
Length of stay, d, median (IQR)	12 (8–20)	7.5 (4–17)	<.01
Source control procedure performed	25 (42.4)	36 (51.4)	.31
Received infectious disease consult	59 (100)	44 (62.9)	<.01
Recommended length of antibiotic course, d, median (IQR)	28 (14–42)	14 (10–42)	<.01
Completed antibiotic course in the hospital	5 (8.6)	12 (17.4)	.15
Prescribed antibiotics at time of discharge	53 (91.4)	58 (84.1)	.22
Route of antibiotics prescribed at discharge			<.01
Oral	49 (92.5)	32 (55.2)	
Intravenous	3 (5.7)	6 (10.3)	
Long-acting intravenous	5 (9.4)	0 (0)	
None: PDD with no antibiotics prescribed	2 (3.8)	21 (36.2)	
Severe infection treated with oral antibiotics[a]	28 (84.8)	9 (31.0)	<.01
Received any MOUD during hospital stay[b]	55 (93.2)	23 (32.9)	<.01
Buprenorphine	53 (89.8)	12 (17.3)	
Methadone	12 (22.0)	12 (17.3)	
MOUD prescribed upon discharge[c]	57 (98.3)	9 (13.2)	<.01
Buprenorphine	55 (94.8)	7 (10.2)	
Methadone	2 (3.5)	2 (2.9)	
Buprenorphine dose prescribed, total milligrams daily, median (IQR)	20 (16–24)	12 (8–16)	.02
Discharged with naloxone	57 (98.3)	0 (.0)	<.01
Discharge disposition			.02
Discharged	48 (81.4)	43 (61.4)	
In-hospital death	1 (1.7)	1 (1.4)	
PDD	10 (17.0)	26 (37.1)	
Discharge location			.04
Private residence or shelter	22 (37.9)	23 (33.3)	
Street/homelessness	15 (25.9)	28 (40.6)	
Residential addiction treatment	16 (27.6)	7 (10.1)	
Salvation Army program or nursing facility	5 (8.6)	10 (14.5)	

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: IQR, interquartile range; MOUD, medication for opioid use disorder; PDD, patient-directed discharge; SIRI, severe injection-related infection.

[a]Denominator is number of patients in each group with severe infection: SIRI team, 33; control group, 29.

[b]Receipt of at least 1 dose of methadone or buprenorphine, among those with opioid use disorder.

[c]One patient in the SIRI team group and 2 in the control group were discharged with plans to continue attending a methadone program; all others were prescribed buprenorphine.

displaying a significantly higher rate of being alive and without hospital readmission at 90 days ($P = .01$). A Kaplan-Meier survival curve for the subset of patients with severe infections showed similar outcomes in the SIRI team group (Supplementary Figure 1). More detailed SIRI team patient outcomes, reasons for readmission, emergency department utilization, and oral antibiotic therapy information are presented in Supplementary Tables 1–4.

DISCUSSION

In this study of patients hospitalized with IDU-associated infections, an integrated ID/SUD clinical team and postdischarge follow-up intervention was associated with a 20% absolute reduction in the risk of readmission or death 90 days after hospital discharge compared to a historical control group. We observed secondary improvements in SUD care engagement and antibiotic completion as well as decreased rates of PDD. Between 2011 and 2018, the estimated number of PWID in the US increased by 5-fold to 3.7 million people [27]. The consequence of this trend is demonstrated by surging rates of drug overdose deaths [2]. Based on the increase in PWID experiencing SIRI and the large preliminary effect size demonstrated with the SIRI team intervention, these data support further evaluation and development of integrated ID/SUD care [11].

The National Academies of Sciences, Engineering and Medicine refer to OUD and infectious diseases as "inextricably linked" and suggest that an integrated approach is required to address the syndemic [28]. These data demonstrate the potential impact of a comprehensive intervention for PWID hospitalized with infections that harnesses the benefits of MOUD, partial oral antibiotic treatments, harm reduction, and intensive postdischarge follow-up. The 90-day readmission rate of our intervention (17%) was lower to that seen among other studies [12]. Previous evaluations of individual components of the SIRI team intervention and have shown favorable results in each case, including MOUD for persons with SIRI [18, 29–31], MOUD plus outpatient parenteral antimicrobial therapy (OPAT) for persons with SIRI [32], partial oral antibiotics for those with SIRI [12, 33], addiction medicine consultation [16], and patient navigation for hospitalized persons with SUD [34]. We showed improvements in outcomes relevant both to patients and health systems alike: decreased readmission rate, PDD rate, ED visits, and days spent in the hospital after discharge as well as increased MOUD initiation, MOUD continuation on discharge, and increased antibiotic completion.

While the SIRI team intervention as a complete package was associated with improvements in care outcomes, it is important to understand what core components of the treatment led to its success. In our study, the control group had a very low rate of MOUD initiation and prescription at discharge. Other studies have shown that MOUD is associated with improvements in both infection, OUD, and healthcare utilization outcomes among persons hospitalized with SIRI [17, 18, 29–31]. Similarly, posthospital care engagement has been associated with reduced readmissions among persons with SIRI [12]; intervention group patients having frequent posthospital physician contact may have also contributed to the successful outcomes. Compared to the control group, SIRI team patients had lower rates of discharge to homelessness and higher rates of residential addiction treatment. Preventing the known harms of homelessness among persons with SUD is a third potential contributor to the intervention's impact [35]. Additionally, SIRI team patients identified trust in the team, harm reduction focus, patient advocacy, and nonstigmatizing care as strengths

Table 3. Primary and Secondary Posthospitalization Outcomes: Unadjusted and Adjusted Relative Risk Ratios

Outcomes	SIRI Team	Control	RR	(95% CI)	aRR[a]	(95% CI)
Primary outcome						
90-d death or readmission	14 (24.1)	30[b] (43.5)	**0.56**	**(.33–.94)**	**0.55**	**(.32–.95)**
Secondary outcomes						
90-d readmission	10 (17.2)	29 (42.0)	**0.41**	**(.23–.77)**	**0.43**	**(.22–.81)**
Postdischarge mortality at 90 d	4 (6.9)	4 (5.8)	1.19	(.31–4.55)	1.17	(.27–5.12)
Antibiotic course completion	53 (89.8)	42 (60.0)	**1.47**	**(1.20–1.81)**	**1.47**	**(1.19–1.82)**

Bold values represent $P < .05$.

Abbreviations: aRR, adjusted relative risk ratio; CI, confidence interval; RR, relative risk ratio; SIRI, severe injection-related infection.

[a]Adjusted for severity of infection.

[b]Three individuals in the control group were readmitted and then died within 90 days of discharge. Only the first event was counted in the composite outcome.

of the intervention, which may have also facilitated the team's effectiveness [36].

The SIRI team prescribed oral antibiotics at high rates (92%) for those who required ongoing treatment at the time of discharge. Studies have shown transition to oral therapy for PWID leaving the hospital to be equally effective to completion of intravenous antibiotics in the hospital [33]. We used a shared decision-making approach [37] with patients, leveraging the strong data for efficacy of oral antibiotics for severe infections, and adapted to PWID [38]. Unsurprisingly, nearly all patients wanted to leave the hospital on oral antibiotics whenever possible and avoid OPAT or prolonged hospitalization. The outcomes observed among our control group patients highlight a false dichotomy that is often made regarding the safety and efficacy of oral versus IV antibiotics among PWID. Some question whether PWID can be adherent to oral antibiotic regimens or if they are better off remaining as inpatients to receive IV therapy. In reality, the calculus is more often oral antibiotics versus the patient leaving the hospital with no treatment at all. We suspect that the 36% of control group

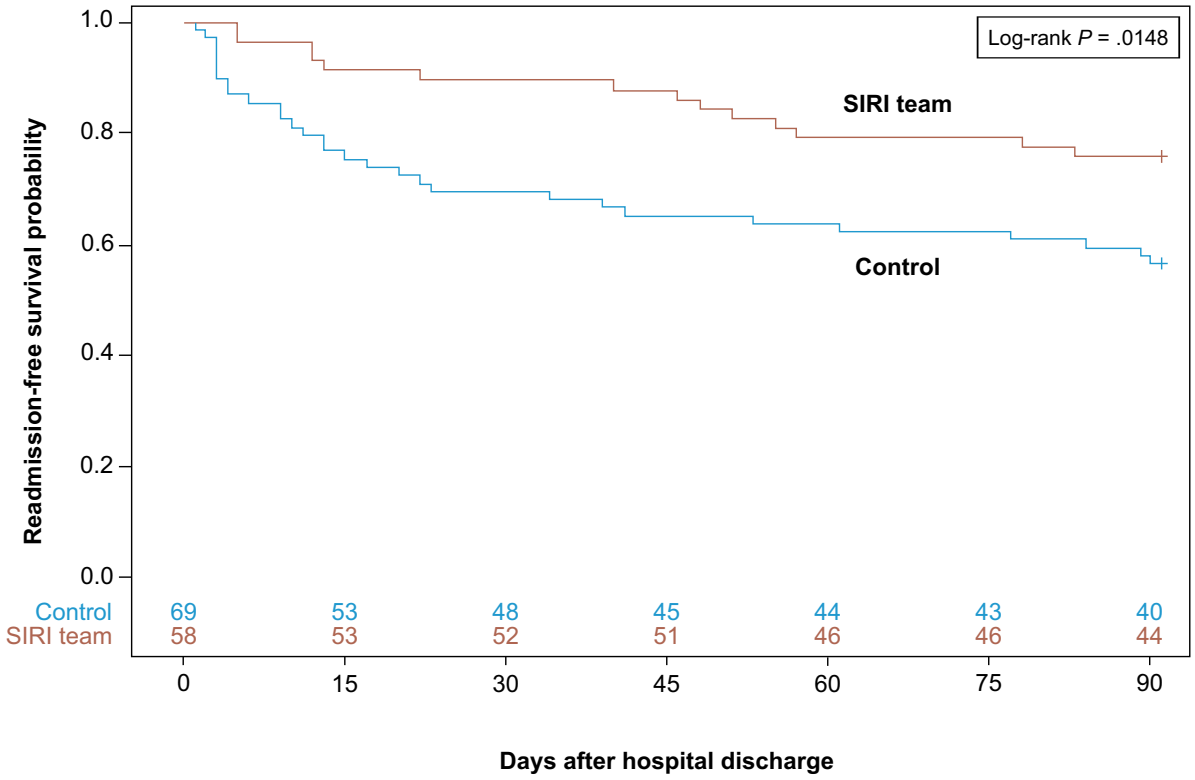

Figure 2. Kaplan-Meier curve of readmission-free survival after hospital discharge between severe injection-related infection (SIRI) team and control patients. Kaplan-Meier survival plot with outcome of alive and free from hospital readmission comparing SIRI team patients to historical control group. Numbers show the sum of patients remaining alive and free from readmission after discharge from initial hospital stay at 15-day increments. All remaining patients were censored at 90 days after hospital discharge.

patients who had an indication for ongoing antibiotics but left under PDD with no therapy contributed to the high readmission rate.

Interpretation of our results requires acknowledgment of several limitations. First, due to lack of randomization and a noncontemporaneous control group, we cannot prove that the intervention definitively caused the improved outcomes observed. Second, unmeasured characteristics, such as income or history of trauma, may have differed between study groups and could confound the association between intervention and outcome. Third, we were unable to estimate the total population of PWID hospitalized with IDU-associated infections during the SIRI team intervention phase; it is probable that not all patients with SIRI were referred to the SIRI team during the intervention period. These data would have allowed our team to evaluate the reach of the intervention and determine if there were differences between those who did and did not receive SIRI team consultation. Fourth, because the control cohort was retrospective and limited to medical records and Miami-Dade County Medical Examiner documentation, we suspect there was ascertainment bias in out-of-hospital death. For example, of the 4 posthospital deaths among SIRI team patients, only 1 was recorded in the medical record or medical examiner's database, while the rest were known only from discussion with emergency contacts. Because all readmission data were abstracted from the medical record of Jackson Memorial Hospital, readmissions to other healthcare facilities were not available for either study group. A few SIRI team patients mentioned seeking healthcare elsewhere during the follow-up period, but because the data were not recorded consistently, they were not included. Finally, external validity of the study is limited by a unique care environment at the implementing institution: other sites may not have access to a closely affiliated SSP including a team of patient navigators/harm reduction counselors. In contrast, other health system contexts with addiction medicine consult teams, expanded Medicaid access, and a stronger social safety net may diminish the added value of an integrated ID/SUD team.

CONCLUSIONS

To date, the healthcare system has failed PWID, particularly those experiencing life-threatening infections [39]. In this study we showed that integration of ID treatment with harm reduction services, including access to lower-barrier SUD treatment and oral antibiotics, was associated with improvements in readmission-free survival among PWID hospitalized with IDU-associated infections. These promising data should promote further testing of the SIRI team intervention in a randomized controlled trial in diverse healthcare systems.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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References

1. McCarthy NL, Baggs J, See I, et al. Bacterial infections associated with substance use disorders, large cohort of United States hospitals, 2012–2017. Clin Infect Dis **2020**; 71:e37–44.
2. Centers for Disease Control and Prevention. NVSS vital statistics rapid release: provisional drug overdose death counts 2022. Available at: https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm. Accessed July 1, 2022.
3. Gonsalves GS, David Paltiel A, Thornhill T, et al. The dynamics of infectious diseases associated with injection drug use in Lawrence and Lowell, Massachusetts. Open Forum Infect Dis **2021**; 8:ofab128.
4. King C, Cook R, Korthuis PT, Morris CD, Englander H. Causes of death in the 12 months after hospital discharge among patients with opioid use disorder. J Addict Med **2022**; 16:466–9.
5. Barocas JA, Eftekhari Yazdi G, Savinkina A, et al. Long-term infective endocarditis mortality associated with injection opioid use in the United States: a modeling study. Clin Infect Dis **2020**; 73:e3661–9.
6. Schranz AJ, Fleischauer A, Chu VH, Wu L-T, Rosen DL. Trends in drug use–associated infective endocarditis and heart valve surgery, 2007 to 2017: a study of statewide discharge data. Ann Intern Med **2019**; 170:31–40.
7. Leahey PA, LaSalvia MT, Rosenthal ES, Karchmer AW, Rowley CF. High morbidity and mortality among patients with sentinel admission for injection drug use–related infective endocarditis. Open Forum Infect Dis **2019**; 6:ofz089.
8. Bearnot B, Mitton JA, Hayden M, Park ER. Experiences of care among individuals with opioid use disorder-associated endocarditis and their healthcare providers: results from a qualitative study. J Subst Abuse Treat **2019**; 102:16–22.
9. Gilbert AR, Hellman JL, Wilkes MS, Rees VW, Summers PJ. Self-care habits among people who inject drugs with skin and soft tissue infections: a qualitative analysis. Harm Reduct J **2019**; 16:69.
10. McNeil R, Small W, Wood E, Kerr T. Hospitals as a 'risk environment': an ethno-epidemiological study of voluntary and involuntary discharge from hospital against medical advice among people who inject drugs. Soc Sci Med **2014**; 105:59–66.
11. Serota DP, Barocas JA, Springer SA. Infectious complications of addiction: a call for a new subspecialty within infectious diseases. Clin Infect Dis **2020**; 70:968–72.
12. Lewis S, Liang SY, Schwarz ES, et al. Patients with serious injection drug use-related infections who experience patient-directed discharges on oral

antibiotics have high rates of antibiotic adherence but require multidisciplinary outpatient support for retention in care. Open Forum Infect Dis **2022**; 9:ofab633.
13. Fanucchi LC, Walsh SL, Thornton AC, Lofwall MR. Integrated outpatient treatment of opioid use disorder and injection-related infections: a description of a new care model. Prev Med **2019**; 128:105760.
14. Weimer MB, Falker CG, Seval N, et al. The need for multidisciplinary hospital teams for injection drug use–related infective endocarditis. J Addict Med **2022**; 16:375–8.
15. Paras ML, Wolfe SB, Bearnot B, et al. Multidisciplinary team approach to confront the challenge of drug use–associated infective endocarditis. J Thorac Cardiovasc Surg **2021**. doi: 10.1016/j.jtcvs.2021.10.048 [Online ahead of print].
16. Marks LR, Munigala S, Warren DK, Liang SY, Schwarz ES, Durkin MJ. Addiction medicine consultations reduce readmission rates for patients with serious infections from opioid use disorder. Clin Infect Dis **2019**; 68:1935–7.
17. Nolan NS, Marks LR, Liang SY, Durkin MJ. Medications for opioid use disorder associated with less against medical advice discharge among persons who inject drugs hospitalized with an invasive infection. J Addict Med **2021**; 15:155–8.
18. Barocas JA, Morgan JR, Wang J, McLoone D, Wurcel A, Stein MD. Outcomes associated with medications for opioid use disorder among persons hospitalized for infective endocarditis. Clin Infect Dis **2021**; 72:472–8.
19. Wakeman SE, Metlay JP, Chang Y, Herman GE, Rigotti NA. Inpatient addiction consultation for hospitalized patients increases post-discharge abstinence and reduces addiction severity. J Gen Intern Med **2017**; 32:909–16.
20. Jo Y, Nosal R, Vittori A, et al. Effect of initiation of medications for opioid use disorder on hospitalization outcomes for endocarditis and osteomyelitis in a large private hospital system in the United States, 2014–2018. Addiction **2021**; 116: 2127–34.
21. Hawk M, Coulter RW, Egan JE, et al. Harm reduction principles for healthcare settings. Harm Reduct J **2017**; 14:1–9.
22. Campanile Y, Silverman M. Sensitivity, specificity and predictive values of *ICD-10* substance use codes in a cohort of substance use-related endocarditis patients. Am J Drug Alcohol Abuse **2022**; 48:1–10.
23. Marks LR, Nolan NS, Jiang L, Muthulingam D, Liang SY, Durkin MJ. Use of *ICD-10* codes for identification of injection drug use-associated infective endocarditis is nonspecific and obscures critical findings on impact of medications for opioid use disorder. Open Forum Infect Dis **2020**; 7:ofaa414.
24. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform **2009**; 42:377–81.
25. Serota DP, Tookes HE, Hervera B, et al. Harm reduction for the treatment of patients with severe injection-related infections: description of the Jackson SIRI team. Ann Med **2021**; 53:1960–8.
26. Chen W, Qian L, Shi J, Franklin M. Comparing performance between log-binomial and robust Poisson regression models for estimating risk ratios under model misspecification. BMC Med Res Methodol **2018**; 18:63.
27. Bradley H, Hall E, Asher A, et al. Estimated number of people who inject drugs in the United States. Clin Infect Dis **2022**:ciac543. doi: 10.1093/cid/ciac543.
28. National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on the Examination of the Integration of Opioid and Infectious Disease Prevention Efforts in Select Programs. Opportunities to improve opioid use disorder and infectious disease services: integrating responses to a dual epidemic. Washington, DC: National Academies Press; **2020**.
29. Marks LR, Munigala S, Warren DK, et al. A comparison of medication for opioid use disorder treatment strategies for persons who inject drugs with invasive bacterial and fungal infections. J Infect Dis **2020**; 222(Suppl_5):S513–20.
30. Kimmel SD, Walley AY, Li Y, et al. Association of treatment with medications for opioid use disorder with mortality after hospitalization for injection drug use–associated infective endocarditis. JAMA Netw Open **2020**; 3:e2016228.
31. Barocas JA, Gai MJ, Amuchi B, Jawa R, Linas BP. Impact of medications for opioid use disorder among persons hospitalized for drug use–associated skin and soft tissue infections. Drug Alcohol Depend **2020**; 215:108207.
32. Fanucchi LC, Walsh SL, Thornton AC, Nuzzo PA, Lofwall MR. Outpatient parenteral antimicrobial therapy plus buprenorphine for opioid use disorder and severe injection-related infections. Clin Infect Dis **2020**; 70:1226–9.
33. Marks LR, Liang SY, Muthulingam D, et al. Evaluation of partial oral antibiotic treatment for persons who inject drugs and are hospitalized with invasive infections. Clin Infect Dis **2020**; 71:e650-e6.
34. Gryczynski J, Nordeck CD, Welsh C, Mitchell SG, O'Grady KE, Schwartz RP. Preventing hospital readmission for patients with comorbid substance use disorder: a randomized trial. Ann Intern Med **2021**; 174:899–909.
35. Fine DR, Dickins KA, Adams LD, et al. Drug overdose mortality among people experiencing homelessness, 2003 to 2018. JAMA Netw Open **2022**; 5:e2142676.
36. Seo G. Implementation of an integrated infectious disease and substance use disorder team for injection drug use–associated infections: a qualitative study. In: IDWeek, Washington, DC, 19–23 October **2022**.
37. Barry MJ, Edgman-Levitan S. Shared decision making—pinnacle of patient-centered care. N Engl J Med **2012**; 366:780–1.
38. Serota DP, Chueng TA, Schechter MC. Applying the infectious diseases literature to people who inject drugs. Infect Dis Clin North Am **2020**; 34:539–58.
39. Eaton EF. We thought we created a safety net. We were wrong. Clin Infect Dis **2021**; 73:e1658–60.