Title

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Journal

The American Journal of Medicine, 135(1)

ISSN

0002-9343

Authors

Appa, Ayesha
Adamo, Meredith
Le, Stephenie
et al.

Publication Date

2022

DOI

10.1016/j.amjmed.2021.08.007

Peer reviewed

HHS Public Access

Author manuscript

Am J Med. Author manuscript; available in PMC 2024 November 11.

Published in final edited form as:

Am J Med. 2022 January ; 135(1): 91–96. doi:10.1016/j.amjmed.2021.08.007.

Patient-Directed Discharges Among Persons Who Use Drugs Hospitalized with Invasive *S. aureus* Infections: Opportunities for Improvement

Ayesha Appa, MD[1], **Meredith Adamo, MD**[2], **Stephenie Le, MD**[2], **Jennifer Davis, MD**[2], **Lisa Winston, MD**[1], **Sarah B. Doernberg, MD, MAS**[3], **Henry Chambers, MD**[1], **Marlene Martin, MD**[2], **Nancy K. Hills, PhD**[2], **Phillip Coffin, MD, MIA**[4], **Vivek Jain, MD, MAS**[1]

[1]Division of HIV, Infectious Diseases & Global Medicine, San Francisco General Hospital, University of California, San Francisco (UCSF), San Francisco, CA, USA

[2]Department of Medicine, University of California San Francisco (UCSF), San Francisco, CA, USA

[3]Division of Infectious Diseases, University of California, San Francisco (UCSF), San Francisco, CA, USA

[4]San Francisco Department of Public Health, San Francisco, CA, USA

Abstract

Background: Despite the high burden of *Staphylococcus aureus* infections among persons who use drugs, limited data exist comparing outcomes of patient-directed discharge (also known as "against medical advice") vs. standard discharge among persons who use drugs hospitalized with *S. aureus* infection.

Methods: We conducted a retrospective study of hospitalizations among adults with *S. aureus* bacteremia, endocarditis, epidural abscess, and/or vertebral osteomyelitis at two San Francisco hospitals between 2013–2018. We compared odds of one-year readmission for infection persistence/recurrence and one-year mortality via multivariable logistic regression models adjusting for age, sex, Charlson comorbidity index and homelessness.

Results: Overall, 80/340 (24%) of hospitalizations for invasive *S. aureus* infections among persons who use drugs involved patient-directed discharge. Over half of patient-directed discharges 41/80 (51%) required readmission for persistent/recurrent *S. aureus* infection vs. 54/260 (21%) patients without patient-directed discharge (adjusted odds ratio 3.8 [95% CI 2.2-6.7]). One-year cumulative mortality was 15% after PDD vs. 11% after standard discharge (p=0.02); however, this difference was not significant after adjustment for mortality risk factors. More than half of deaths in the patient-directed discharge group (7/12, 58%) were due to drug overdose; none was due to *S. aureus* infection.

Corresponding Author: Ayesha Appa, MD, Division of HIV, Infectious Diseases & Global Medicine, Zuckerberg San Francisco General Hospital and Trauma Center, University of California, San Francisco (UCSF), 995 Potrero Avenue, Building 80, Box 0874, San Francisco, CA 94110, Ayesha.appa@ucsf.edu.

All authors were able to access study data and contributed to the study design, data acquisition, analysis, writing and/or editing of this manuscript.

Conclusions: Among persons who use drugs hospitalized with invasive *S. aureus* infection, odds of hospital readmission for infection were almost 4-fold higher following patient-directed discharge compared to standard discharge. All-cause one-year mortality was similarly high in both groups, and drug overdose was a common cause of death in patient-directed discharge group.

Keywords

Staphylococcus aureus; staphylococcal infections; patient discharge; patient readmission; drug overdose

INTRODUCTION

Invasive *Staphylococcus aureus* infections associated with drug use are increasingly common causes of hospitalization [1-4]. Persons who use drugs hospitalized with invasive *Staphylococcus aureus* infections also face elevated and increasing rates of patient-directed discharge, “against medical advice”. [5-7] A recent study found that odds of patient-directed discharge during hospitalization for drug use-related endocarditis have been increasing 12% per year nationwide.[8] These interrupted acute care episodes are associated with patient dissatisfaction and distrust of healthcare institutions [9], elevated 30-day hospital readmission rates [10-14], and in some studies, higher 30-day mortality. [11,13]

Despite the rising numbers of persons who use drugs with invasive *S. aureus* infections and rising patient-directed discharge, limited data compare infection outcomes, including mortality, of persons who use drugs with invasive *S. aureus* infections that end in patient-directed discharge vs. standard discharge. Thus, we compare demographics, substance use characteristics, hospital readmission rates and mortality rates between persons who use drugs with and without patient-directed discharge hospitalized with invasive *S. aureus* infection.

METHODS

Study Design, Setting, and Participants

We performed a retrospective cohort study of patients hospitalized from 2013-2018 at two hospitals, San Francisco General Hospital (226-bed public county hospital/trauma center) and UCSF Medical Center (839-bed tertiary care/referral hospital).

We previously described the patient cohort [15]; briefly, we identified 1,011 hospitalizations among adults during which a microbiologic diagnosis of invasive *S. aureus* infection (defined as bacteremia, endocarditis, epidural abscess, and/or vertebral osteomyelitis) was made via strutured chart review. For this analysis, we included only persons who use drugs and excluded hospitalizations that did not involve an invasive *S. aureus* infection or where *S. aureus* was designated a contaminant. In the present analysis of post-hospital discharge outcomes, we also excluded hospitalizations in which patients died or transitioned to comfort-focused care in the hospital. Our final sample consisted of 340 adult hospitalizations for invasive *S. aureus* infection.

Definitions

Four co-authors (AA, MA, SL, JD) performed structured chart reviews. We jointly reviewed a subset of charts to assure precision in data extraction. We defined persons who use drugs as patients with any non-prescribed substance use noted in hospital records of the primary team, infectious diseases consultants, or social workers. Cannabis, alcohol, and tobacco use were excluded. We defined patient-directed discharge as occurring "against medical advice" (or with synonymous terms, e.g., "AMA," or "AWOL") in hospital discharge records or other documentation. Using electronic medical record (EMR) data including data obtained from CareEverywhere (Epic Systems), we ascertained 30-day and one-year readmission to any area hospital for ongoing or recurrent *S. aureus* infection. One-year all-cause mortality was ascertained both by chart review and cross comparison to the California state death registry.[16] We reviewed causes of death occurring <1 year after hospital discharge. Out-of-state patient deaths were not captured. We recorded patient-directed discharge reasons described in hospital records and identified common themes.

Statistical Analysis

We compared demographic, clinical and substance use features between persons who use drugs with and without patient-directed discharge using Chi-square tests. Adjusted odds of one-year readmission for infection recurrence or persistence, as well as one-year all-cause mortality, were compared between groups using a multivariate logistic regression model adjusted for age, race, housing status, medical co-morbidities, and methicillin-resistant vs. methicillin-sensitive *S. aureus* (MRSA vs. MSSA) infection.

Ethics Statement

The study was approved by the University of California, San Francisco Committee on Human Subjects Research.

RESULTS

Overall, 80/340 (24%) hospitalizations for invasive *S. aureus* infection among persons who use drugs ended in a patient-directed discharge. Compared to persons who use drugs with a standard discharge, persons who use drugs with patient-directed discharge were younger (median age 44 vs. 52 years), more likely to be experiencing homelessness (59% vs. 31%), less chronically ill (median Charlson comorbidity score 1 vs. 2), and more likely to be living with HIV (26% vs. 17%; Table 1). Substance use characteristics also differed between patients with patient-directed discharge vs standard discharges. Compared to standard discharge patients, patients with self-directed discharge were more likely to report injection drug use (83% vs. 67%), opioid use (69% vs. 54%), methamphetamine use (61% vs. 47%), and combined opioid and stimulant use (see Table 1).

Infection type (bacteremia, endocarditis, vertebral osteomyelitis, and epidural abscess) and drug resistance pattern (MRSA vs. MSSA) were similar between groups (Table 1). Intensive care unit admission was less common among patient-directed discharge vs. standard discharge patients (18% vs. 40%). Receipt of surgical source control of infection was also less common among patient-directed discharge patients (41% vs. 56%). Fewer patient-

directed discharge vs. standard discharge patients received peripherally inserted central catheters (PICC; 51% vs. 71%; p <0.01). Finally, in both patient-directed discharge and standard discharge patients using opioids, initiation of methadone or buprenorphine occurred in less than half of the patient-directed discharge group (47%) and standard discharge group (42%).

Unadjusted outcomes of invasive *S. aureus* infections among persons who use drugs with a patient-directed discharge are shown in Table 2. Only 11% of planned antibiotic treatment courses were completed by persons who use drugs with patient-directed discharge, compared to 88% antibiotic completion in the standard discharge group (p <0.01). In total, 44/80 (55%) of persons who use drugs with patient-directed discharge were readmitted to the hospital ≤30 days after discharge versus 47/260 (18%) of persons who use drugs with standard discharges (p <0.01). Overall, 39/44 (89%) of 30-day readmissions after patient-directed discharge were for persistent or recurrent *S. aureus* infection, compared to only 20/47 (43%) of 30-day readmissions following standard discharge. In a multivariable model adjusted for age, race/ethnicity, Charlson comorbidity score, and housing status, adjusted odds of readmission for infection in the patient-directed discharge group vs. standard discharge group was 3.8 (95% CI 2.2-6.6, Table 3).

Cumulative mortality by one year following discharge was 15% among patient-directed discharge group vs. 11% in the standard discharge group (p=0.02). While unadjusted mortality was higher in the patient-directed discharge group, adjusted analysis showed odds of death were not different between groups (OR 1.5 [0.7 – 3.3], Table 3). Of the 12 deaths in the patient-directed discharge group, none was due to *S. aureus* or other bacterial infection. More than half of deaths (7/12, 58%) were due to drug overdose. Of the 28 deaths in the standard discharge group, 5/28 (18%) were due *S. aureus* infection, and 4/28 (14%) were due to drug overdose.

Review of the top causes of patient-directed discharge revealed five categories: (1) housing concerns and/or caring for dependents (n=13), (2) social isolation in the hospital (n=11); (3) being suspected of using drugs in the hospital (n=11), (4) stigmatizing behaviors by hospital providers and staff (room searches, video surveillance, and other restrictive measures, n=11), and (5) undertreated pain (n=7). In 24 patients, no reason for patient-directed discharge was available in hospital records.

DISCUSSION

In a large cohort of persons who use drugs hospitalized with an invasive *S. aureus* infection, patient-directed discharge was higher among patients with younger age, persons using injection drugs (particularly opioids and methamphetamine), and persons experiencing homelessness. Patient-directed discharge was associated with almost four-fold increased odds of readmission within one year for infection compared to persons who use drugs with a standard discharge. All-cause mortality was similarly high in both discharge groups (more than 1 in 10 persons who use drugs died within a year of *S. aureus* infection hospitalization), but most deaths in the patient-directed discharge group were due to drug overdose, rather than untreated infection. Most commonly documented reasons for patient-directed discharge

included logistic demands outside of the hospital and stigmatizing experiences during hospitalization.

Thirty-day readmission rates following patient-directed discharge during infection treatment are consistently elevated across studies [12,17-19], indicating the potential for ineffective treatment. Our findings of high 30-day and one-year readmission rates among persons who use drugs with patient-directed discharge are consistent with existing data. Additionally, we found that readmission for *S. aureus* infection among persons who use drugs was <10% in the first month after standard discharge but almost 50% in the month following patient-directed discharge. While we are unable to definitively distinguish between ongoing and recurrent infection, this temporality suggests that a priority issue to address is interrupted antibiotic treatment.

Developing more effective, patient-centered treatment plans may be effective in averting patient-directed discharge and antibiotic treatment interruption. Important options include home-based outpatient parenteral antibiotics, known to be preferred by patients [20] yet heavily underutilized in persons who use drugs [21], or oral antibiotic regimens when appropriate. Marks, et al. demonstrated that prescription of oral antibiotics at time of patient-directed discharge during hospitalization for infection was associated with decreased readmission rates compared to patient-directed discharge without oral antibiotics. [22] Relatedly, expanding literature supports oral antibiotic regimens for many deep-seated infections [23,24]. However, persons who use drugs are often excluded from these studies, which has limited their generalizability. Our study suggests that targeting antibiotic treatment interruption with innovative care delivery models might offer a pathway to reduced readmission rates and foster more patient-centered care for persons who use drugs.

Despite the substantial morbidity associated with patient-directed discharge, we did not observe increased one-year all-cause mortality among patient-directed discharge patients versus standard discharge patients. No deaths in the patient-directed discharge group were caused by untreated *S. aureus* infection—most were due to drug overdose. Our findings are consistent with mixed literature on this topic. Two large cohort studies of hospital discharges in the Veteran's Administration system [11] and in one urban center [13] demonstrated increased odds of 30-day mortality following patient-directed discharge compared to standard discharge. However, other studies specific to infection (e.g. drug use-associated endocarditis) have demonstrated either similar or reduced mortality associated with patient-directed discharge. [25-27] It is likely that lower age, and lower frequency of comorbidities and critical illness in the patient-directed discharge group have mitigated mortality. That said, we found that one-year all-cause mortality was strikingly high in both groups of persons who use drugs, particularly considering our population was relatively young and had relatively few comorbid illnesses. Among deaths in the patient-directed discharge group, more than half (58%) were due to fatal drug overdose, while no deaths were due to untreated *S. aureus* infection. Our findings indicate that, in addition to formulating effective antibiotic treatment plans with patients, addressing substance use disorders during hospitalization is of utmost importance. Hospitalization represents a "reachable moment" for patients interested in changing their substance use [28]; in addition, fatal overdose risk is known to be elevated following hospitalization. [29]

Reasons for patient-directed discharge in our study raise questions about the nature and patient-centeredness of hospital care, suggesting opportunities for improvement. First, the burden of competing life priorities such as maintaining shelter or caring for dependents, for persons who use drugs who experience overlapping challenges of mental health conditions, poverty, homelessness, and structural racism may interfere with the ability to complete prolonged parenteral antibiotic therapy. This is another call for tailoring antibiotic delivery to the unique needs of persons who use drugs. Second, our data suggest that stigma towards persons who use drugs, including room searches or video surveillance, need to be addressed as a cause for patient-directed discharge. Our data are consistent with qualitative studies of patient perspectives on patient-directed discharge.[31,32] Simon et al. cited stigma and discrimination by hospital staff as a common contributor to patient-directed discharge, along with undertreated withdrawal, substance cravings, untreated pain, and restrictive policies. While much existing literature on patient-directed discharge identifies patient characteristics that raise the risk of patient-directed discharge, our data emphasize the need to also identify reasons for patients leaving that are rooted in processes of healthcare systems.

Our study was subject to certain limitations. First, this is a retrospective study of persons who use drugs admitted to two San Francisco hospitals, so regional patterns of drug use and local or institutional factors may limit generalizability to other locations. Second, comparative data on care utilization (e.g. receipt of PICC line, surgery, etc.) between two groups with different lengths of stay should be interpreted with caution. In many cases, early patient-directed discharge patients did not have the opportunity to be offered surgery. Conversely, not offering some aspects of care may have contributed to a discharge. Finally, the reported reasons for patient-directed discharge were recorded based upon chart review, rather than direct qualitative data directly obtained from patients. As such, information may be incomplete and may not capture the full range of patient and provider perspectives.

In conclusion, among persons who use drugs hospitalized with invasive *S. aureus* infection, patient-directed discharge was associated with markedly increased odds of one-year readmission. All-cause mortality was relatively similar between patient-directed discharge and standard discharge groups, with a stark toll of drug overdose deaths in the patient-directed discharge group. Among persons who use drugs who are younger, often using opioids and methamphetamine, and experiencing homelessness, there is an urgent and growing need to develop, test, and implement novel patient-centered therapeutic strategies that prevent patient-directed discharges, allow for completion of infection therapy, and mitigate morbidity when patient-directed discharges occur.

Sources of Funding:

This work was supported by the National Institutes of Health grants 5T32AI007641-17 (AA), K24DA042720 (PC), and R25DA033211 (AA).

Declaration of Interest:

Authors SD and HC disclose an unrelated source of funding National Institutes of Health grant UM1AI104681, and SD discloses receipt of consulting fees from Genentech and Basilea Pharmaceutica, though unrelated to this work. None of the remaining authors of conflicts of interest to disclose.

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Table 1.

Demographic, clinical, substance use, and hospitalization characteristics among persons who use drugs, stratified by patient-directed discharge

	Patient-directed Discharge* N=80	Standard Discharge N=260	P-value†
Demographic			
Age (median, IQR)	44 (33-52)	52 (42-57)	<0.01‡
Male sex (n, %)	50 (63%)	189 (73%)	0.08
Race/ethnicity			0.27
White	51 (64%)	149 (57%)	
Black/African American	13 (16%)	57 (22%)	
Hispanic/Latinx	6 (8%)	35 (14%)	
Asian/Pacific Islander	3 (4%)	5 (2%)	
Other	7 (9%)	14 (5%)	
Experiencing homelessness (%, n)	47 (59%)	81 (31%)	<0.01
Clinical			
Charlson comorbidity score (median, IQR)	1 (0-2)	2 (1-4)	<0.01‡
HIV positive	21 (26%)	43 (17%)	0.03
Immunosuppressed§ (%, n)	22 (28%)	51 (20%)	0.13
Any mental health condition (%, n)	30 (38%)	89 (34%)	0.59
Substance Use			
Injection route described (%, n)	66 (83%)	176 (68%)	0.04
Recent drug use (<1 mo) (%, n)	75 (94%)	170 (65%)	<0.01
Drug type (%, n)			
Heroin	51 (64%)	132 (51%)	0.04
Any opioid	55 (69%)	141 (54%)	0.02
Cocaine	24 (30%)	101 (39%)	0.15
Methamphetamine	49 (61%)	123 (47%)	0.03
Opioid and stimulant	39 (49%)	93 (36%)	0.04
Unhealthy alcohol use¶ (%, n)	10 (13%)	54 (21%)	0.20
Hospitalization			
MRSA infection	46 (58%)	119 (46%)	0.07
Type of infection (%, n)			
Bacteremia	60 (75%)	197 (76%)	0.89
Endocarditis	17 (21%)	47 (18%)	0.62
Vertebral osteomyelitis	19 (24%)	80 (31%)	0.23
Epidural abscess	15 (19%)	74 (28%)	0.08
ICU admission during hospital course	14 (18%)	105 (40%)	<0.01
Surgical source control performed	33 (41%)	145 (56%)	0.02

	Patient-directed Discharge* N=80	**Standard Discharge N=260**	**P-value†**
PICC placed#	38/75 (51%)	164/232 (71%)	<0.01
Inpatient MOUD received**			0.51
None	26 (47%)	59 (42%)	
New methadone start	15 (27%)	30 (21%)	
New buprenorphine start	1 (2%)	5 (4%)	
Prior MOUD continued	13 (24%)	46 (33%)	

*Also known as against medical advice.

†P-values were calculated using chi-square tests unless otherwise indicated.

‡P-value calculated using Wilcoxon rank sum test.

§Immunosuppressed defined as those with HIV, chronic exposure to daily prednisone 10mg or more, biologic agents or DMARDs, hematologic malignancy, or chemotherapy.

¶Diagnosed with alcohol use disorder or noted to consume more than 3 or 4 alcoholic drinks daily in women and men respectively.

#Of people eligible for PICC placement (i.e. excluding people with pre-existing central access).

**Of those who reported opioid use.

Table 2:

Unadjusted outcomes of invasive *S. aureus* infection in persons who use drugs, by patient-directed discharge vs. standard discharge

Unadjusted Outcomes	**Patient-directed Discharge[*] N=80**	**Standard Discharge N=260**	**P-value[†]**
Completed planned antibiotic treatment (%, n)	9 (11%)	230 (88%)	<0.01
30-day hospital readmission (overall)	44 (56%)	47 (18%)	<0.01
30-day hospital readmission for infection	39 (49%)	20 (8%)	<0.01
One-year hospital readmission for infection	42 (53%)	57 (23%)	<0.01
One-year all-cause mortality[‡]	12 (15%)	28 (11%)	0.02

[*] Also known as against medical advice.

[†] P-values were calculated using chi-square tests unless otherwise indicated.

[‡] P-value calculated using Fisher's exact test. Category consists of those who survived to hospital discharge, not on hospice.

Table 3:

Odds of readmission among persons who use drugs for persistent/recurrent infection or mortality one year after patient-directed discharge vs. standard discharge

	One-year hospital readmission for infection OR (95% CI)	One-year all-cause mortality OR (95% CI)
Unadjusted	4.0 (2.3 - 6.7)	1.5 (0.7 - 3.0)
Adjusted for age, race/ethnicity, Charlson Comorbidity score, and housing status	3.8 (2.2 - 6.7)	1.5 (0.7 - 3.3)