

Oregon Health & Science University
School of Medicine

Scholarly Projects Final Report

Title

Staphylococcus aureus Bacteremia: Does Intravenous Drug Use Impact Quality of Care or Clinical Outcomes?

Student Investigator's Name

Kristen McClellan

Date of Submission

03/09/2022

Graduation Year

2022

Project Course

Scholarly Projects Curriculum

Co-Investigators

Cami Hilsendager, MD, The Vancouver Clinic, Vancouver, WA

Luke Strnad, MD, Division of Infectious Diseases, OHSU

Mentor's Name

Dr. Luke Strnad

Mentor's Department

Infectious Diseases

Scholarly Project Final Report

Concentration Lead's Name

Dr. Silbert

Project/Research Question

In *Staphylococcus aureus* bacteremia, how do patient demographics, bacteremia characteristics, standards of care metrics, and clinical outcomes differ between persons who do and do not inject drugs?

Type of Project

Research study

Key words

- *Staphylococcus aureus* Bacteremia
- Intravenous Drug Use
- Substance Use Disorder

Meeting Presentations

IDWeek2020, Online due to COVID, October 2020, Recorded poster presentation

Publications

TBD...Working on manuscript now

Submission to Archive

Please hold submission to archive until publication of manuscript.

Scholarly Project Final Report

Next Steps

What are possible next steps that would build upon the results of this project? Could any data or tools resulting from the project have the potential to be used to answer new research questions by future medical students?

Potential future project ideas: Investigating infectious screening in patients admitted with Staph aureus bacteremia and IV drug use from this data set, further characterizing the role of medications for opioid use disorder and the impact on antibiotic completion or patient-directed discharges, creating a more recent database collection and comparing to prior (since IMPACT team well established, OPAT options care conference in place, and possible changes in substances used), creating a QI project for improving antibiotic completion and patient-directed discharges in patients with invasive infections and IV drug use.

Please follow the link below and complete the archival process for your Project in addition to submitting your final report.

https://ohsu.ca1.qualtrics.com/jfe/form/SV_3ls2z8V0goKiHZP

Student's Signature/Date *(Electronic signatures on this form are acceptable.)*

This report describes work that I conducted in the Scholarly Projects Curriculum or alternative academic program at the OHSU School of Medicine. By typing my signature below, I attest to its authenticity and originality and agree to submit it to the Archive.

X

Student's full name

Mentor's Approval *(Signature/date)*

X

Mentor Name

Scholarly Project Final Report

Report:

Introduction

It is well known that injection drug use places individuals at a higher risk for invasive infections^{1,2}. Rates of injection drug use and hospitalizations for serious infections related to the underlying substance use continue to increase nationwide³⁻⁶. In Oregon, where this study takes place, as intravenous drug use rates have risen, bacteremia rates increased most rapidly out of all the intravenous drug use-related infections at 18-times the cases in 2018 when compared to 2008⁴. Since there is also an increased likelihood of *Staphylococcus aureus* infections in persons who inject drugs (PWID), *Staphylococcus aureus* bacteremia (SAB) is an essential disease process to understand in this patient population^{1,7}.

SAB is associated with a high 30-day mortality rate at 15-25%, high healthcare costs, and long hospital stays^{3,4,8}. Studies have demonstrated that PWID with invasive infections tend to be younger with fewer comorbidities, more likely to be infected with MRSA, less likely to complete antibiotics, and more likely to leave the hospital as a patient-directed discharge (PDD; also known as “leaving against medical advice” or “AMA”)⁹⁻¹⁶. Given these unique characteristics in PWID and growing rates of intravenous drug-related SAB, the objective of this study was to compare patient demographics, bacteremia characteristics, adherence to standards of care metrics, and clinical outcomes in patients with SAB who do and do not use intravenous drugs. Given the integrated addiction medicine team at our institution, our study was in a unique position to extract detailed information about substance use and treatment while patients were hospitalized for SAB. We hope to use this information to highlight the unique aspects of SAB in PWID and elucidate areas for potential improvement in clinical care.

Methods

Study Design and Patient Population

This was a single-center retrospective chart review study that was conducted on all cases of SAB between January 1, 2016 and December 31, 2017 at Oregon Health & Science University Hospital, a 500-bed teaching hospital in Portland, Oregon. 285 subjects met inclusion criteria which included age ≥ 18 years old and at least one blood culture positive for *S. aureus*. Patients were excluded if they died, transitioned to comfort care, or transferred hospitals within 48 hours of diagnosis (n=14), had a ventricular assist device infection (n=8), or had no follow-up data at 30-days and 90-days (n=15). A total of 248 patients were included in the final analysis. The study was approved by the Institutional Review Board.

Study Variables and Outcomes

Two authors (C.H., K.M) reviewed the electronic health record for patient demographics, SAB characteristics, metrics of standards of care, clinical outcomes, and if applicable, details of substance use. Substance use data was obtained from detailed addiction medicine and social work notes and included types of substances, diagnosed use disorders, and whether medication for opioid use disorder (MOUD) was initiated. Patient demographics included age, sex, race, and homelessness. Comorbidities such as hepatitis C, HIV, diabetes, hemodialysis, and malignancy were also gathered. Characteristics of SAB included duration of bacteremia, methicillin susceptibility, and complications such as definite and possible endocarditis, spinal epidural abscess/osteomyelitis, skin and soft tissue infection, and deep vein thrombosis/superficial vein thrombosis. “Definite” and “possible” endocarditis was based on modified Duke criteria with the exclusion of fever and intravenous drug use as minor criteria.

Primary outcomes were antibiotic completion and 90-day recurrence, readmission, and mortality. Secondary outcomes included length of hospital stay, patient-directed discharges, and adherence to standards of care. Standards of Care for treatment of SAB were derived from evidence-based guidelines

Scholarly Project Final Report

from the Infectious Diseases Society of America as well as systematic reviews^{17,18}.

The standards of care metrics evaluated in chart review included: repeat of blood cultures until clearance was proved, appropriate antibiotic choice and duration, completion of antibiotic therapy, consultation of infectious diseases, and obtaining a transthoracic or transesophageal echocardiogram^{8,17,19-22}. “Appropriate antibiotic choice” for MSSA was an antistaphylococcal beta-lactam such as nafcillin/oxacillin, cefazolin or if an allergy was present, vancomycin or daptomycin. For MRSA bacteremia, “appropriate antibiotics” included vancomycin, daptomycin with acceptable alternatives of linezolid or ceftaroline. “Appropriate antibiotic duration” was determined by prescribed length of antibiotics based on whether the patient had a complicated or uncomplicated bacteremia. Complicated bacteremia is defined by any of the following factors: endocarditis, implanted prostheses, follow-up cultures remain positive >2-4 days after initial set despite appropriate antibiotics, no defervescence within 72 hours of initiating therapy, or metastatic sites of infection¹⁸. Appropriate duration of complicated bacteremia therapy should be at least 4 weeks, while uncomplicated bacteremia therapy should be at least 14 days¹⁸.

Statistical Analysis

Data were analyzed using SPSS Statistics software (IBM Corp. Released 2019. IBM Statistics for Macintosh, Version 26.0. Armonk, NY: IBM Corp.). Continuous variables were represented as medians or interquartile ranges and analyzed using independent samples t-tests. Categorical data was presented as values and percentages and analyzed by the Pearson Chi-square or Fisher’s exact test, as appropriate. Initially with multivariable analysis, collinearity was assessed to identify potential confounding variables. The best model of fit was determined through model diagnostics. All tests with p-values <0.05 were considered statistically significant.

Results

Patient Demographics and SAB Characteristics

Of the total 248 patients who met inclusion criteria for this study, 28.2% (n=70) were persons who inject drugs. Table 1 compares the patient demographics between PWID and non-PWID. There was a significant statistical difference between PWID and non-PWID in age, homelessness, and comorbidities. The PWID group was younger with a median age of 37 years compared to 57 years in the non-PWID group (p<0.0001). PWID were more likely to experience homelessness (43.3% vs 3.9% in non-PWID, p<0.0001) and have hepatitis C as a comorbidity (53.1% vs. 7.8% in non-PWID, p<0.001). Statistically significant comorbidities for persons without injection drug use compared to PWID included diabetes (31.5% vs. 10.0% p<0.001), hemodialysis (9.0% vs. 0.0%, p=0.01), and malignancy (23.0 vs 1.4%, p<0.001). There was no statistically significant difference between the groups in sex, race, or the comorbidity, HIV.

Staphylococcus aureus bacteremia characteristics of both groups are also displayed in table 1. PWID were more likely to be infected with MRSA (55.7% vs 32.0% in non-PWID, p<0.001) with longer duration of bacteremia (median 4.3 days vs. 2.7 days in non-PWID, p<0.03) and with the complications endocarditis, spinal infections (spinal epidural abscess and osteomyelitis), and skin and soft tissue infections. There was no significant difference between groups in regard to polymicrobial infections and the complication of deep or superficial vein thrombosis.

Substance Use Characteristics and Management in PWID

Within the PWID group, Table 2 presents the details of substance use and management while admitted with SAB. Of those who inject drugs, 84.3% used opioids, 84.3% used methamphetamines, and 71.4% used both opioids and stimulants. 82.8% were diagnosed with an opioid use disorder, 78.9% with a stimulant use disorder, and 42.9% received an inpatient consult with the addiction medicine team. In terms of severity as defined by the DSM-V, 90.6% of the 53 patients with OUD (opioid use disorder) were categorized as

Scholarly Project Final Report

“severe” and 5.7% as “moderate” with 3.8% unknown severity. 86.8% of patients with OUD also reported stimulant use. While hospitalized for SAB treatment, 73.6% of patients with OUD received inpatient medications for opioid use disorder including methadone, buprenorphine and naloxone, or buprenorphine alone. Approximately 17% of patients declined MOUD when offered while inpatient. A MOUD prescription was provided to 30.2% of patients with OUD at discharge.

Adherence to SAB Standards of Care Metrics

Figure 1 compares the adherence to SAB standards of care metrics in persons with and without injection drug use. PWID had lower antibiotic completion rates at 68.1% vs. 84.3% in non-PWID ($p=0.01$). Antibiotic completion rates were lower (62.3%) in PWID with an opioid use disorder ($n=53$). In PWID with an opioid use disorder and stimulant use ($n=46$), antibiotic completion rates were even lower at 60.9%. Fewer transthoracic echocardiograms were performed in non-PWID (82.0%) when compared with PWID (94.3%, $p=0.01$). There was no significant statistical difference in rates of repeat blood cultures until clearance, infectious disease consultation, TEE, or antibiotic choice and duration between groups.

Clinical Outcomes

As table 3 shows, clinical outcomes varied between the PWID and non-PWID group. Univariate analysis revealed PWID was associated with longer hospital stays (median 21.5 days vs. 14 in non-PWID, $p<0.001$), increased patient directed discharges (25.7% vs. 1.1% in non-PWID, $p<0.001$), and lower 90-day mortality (5.7% vs. 18.6% in non-PWID, $p<0.01$). Of PWID, those with opioid use disorders ($n=53$) and opioid disorders with stimulant use ($n=46$) had higher rates of patient-directed discharges at 32.1% and 34.8% respectively. No significant difference was seen in inpatient mortality or 90-day readmission rates between the two groups.

In the multivariable analysis of the full cohort, the failure to complete antibiotics was more likely to occur in intravenous drug use (OR 2.52, 95% CI [1.28, 4.96]) and treatment duration longer than 2 weeks (OR 4.29, 95% CI [1.42, 12.98]) and less likely to occur with infectious diseases consultation (OR 0.15, 95% CI [0.05, 0.51]). Within the PWID cohort, failure to complete antibiotics was less likely with MAT prescribed at discharge (OR 0.03, 95% CI [0.003, 0.339]) and more likely with opioid use disorder (OR 18.38, 95% CI [1.84, 183.92]).

Multivariable analysis of the overall cohort revealed patient directed discharge was associated with PWID (OR 19.22, 95% CI [4.09, 90.28]) and less likely with increasing age (OR 0.963, 95% CI [0.92, 1.01]). In those with PWID, patient directed discharge was associated with hepatitis C virus (OR 4.55, 95% CI [1.30, 15.96]).

Discussion

Overall, this study showed that both PWID and non-PWID received similar treatment of SAB as measured by standards of care metrics such as ID consultation, repeat blood cultures until clearance, and appropriate selection of antibiotic type and duration. These same findings were also demonstrated in a study by Serota et al.⁹. However, when comparing the two groups of patients, there are stark differences in patient demographics, bacteremia characteristics and complications, antibiotic completion rates, patient-directed discharge rates, and 90-day mortality rates. Building upon the existing medical literature about PWID and invasive infections, the findings of this study suggest that within SAB, PWID and non-PWID are distinct populations that can be viewed as different epidemiologies. Describing the differences in PWID and non-PWID within SAB can further inform best practice for approaching treatment for each unique group.

As is consistent with literature about patients with invasive infections, persons who inject drugs are younger with fewer comorbidities when compared to non-PWID^{9,16,23,24}. As is expected with a population that is younger with fewer comorbidities, the 90-day mortality rate was significantly lower in PWID in our study when compared to non-PWID. Appa et al.’s study demonstrated similar results in invasive

Scholarly Project Final Report

Staphylococcus aureus infections and persons who use drugs experienced lower one-year all-cause mortality compared to persons who do not use drugs²³. There was no statistically significant difference in our study with PWID and non-PWID in regards to inpatient mortality rates. This finding may be a reflection of certain unique aspects of PWID such as increased MRSA rates and the higher early mortality associated with MRSA bacteremia as well as unmeasured social determinants of health^{8,20,24-26}. Delayed access or barriers to care could contribute to inpatient mortality rates in PWID, especially since 43.3% were experiencing homelessness. Additionally, PWID was associated with the comorbidity hepatitis C and SAB complications such as osteomyelitis, epidural abscess, and endocarditis, which is consistent with previous findings^{9,16,24}

Other important clinical outcomes for patients with SAB, included a statistically significant lower antibiotic completion rate and increased patient-directed discharges in PWID compared to non-PWID. In the total cohort, PWID had an odds ratio of 2.5 for not completing antibiotics and 19.22 for PDD. Our study had a similar rate of antibiotic completion in PWID (68%) as a previous study (70%)¹⁶ and comparable patient-directed discharge rates in PWID (25.7%) as multiple studies (24-30%)^{9,13,16}.

To our knowledge, this is the first study to show that a MOUD prescription at discharge was associated with improved antibiotic completion in PWID with SAB. A previous study by Marks et al. demonstrated that in PWID with any invasive bacterial or fungal infection, MOUD was associated with increased parenteral antibiotic completion and if continued on discharge, lower 90-day readmissions²⁸. Notably in the Marks et al. study, methadone for the purpose of detoxification that was not continued after discharge was not associated with a reduction in readmissions²⁸. These findings and our results support the important opportunity to utilize the “reachable moment” of inpatient hospitalization for an invasive infection to not only treat the infection, but also the underlying addiction that predisposes patients to that infection through prescribing both inpatient and outpatient MOUD²⁹⁻³¹. At our institution, rates of prescribing MOUD were higher than other studies reported at their institutions^{9,16}. OUD had an odds ratio of 18.38 for not completing antibiotics. Therefore, treating the OUD could help improve this important clinical outcome for patients.

For patient-directed discharges, multivariate analysis demonstrated that hepatitis C in PWID had an odds ratio of 2.55 of PDD. Hepatitis C had collinearity with other variables such as opioid use, homelessness, and DSM-V severity. The presence of hepatitis C was shown to reflect the severity of substance use disorder as a study by Wagner et al. demonstrated that hepatitis C in people who use intravenous drugs was associated with years of injection use, history of non-fatal overdoses, and polysubstance use²⁷. Therefore, hepatitis C could serve as an indicator of higher severity of substance use and thus higher risk for PDD. Other studies have shown that opioid and stimulant use together places people at higher risk for PDD than opioid use alone³². The high rates of stimulant use in our study population could certainly contribute to high PDD rates given there is no highly effective medication therapy for stimulant use disorder. Withdrawal symptoms, untreated pain, and discrimination also lead to high PDD rates in PWID³³.

Both higher PDD rates and lower antibiotic completion rates can explain increased readmission and recurrence rates in PWID, despite the fact this group is younger with fewer comorbidities¹³. While there was no significant statistical difference in recurrence and readmissions at 90 days in the PWID and non-PWID groups, PWID had higher rates of both outcomes and double the rate of SAB recurrence. Beyond therapy completion and PDD, unmeasured social determinants of health may also play a role in increased readmissions and recurrences in this group.

Limitations of our study include that it takes place at one academic center with a small sample size (n=70) of patients with SAB and intravenous drug use. Since the study is in Portland, OR our cohort is mostly white and there is a high rate of stimulant use, so certain elements of this population is not reflective of the data in other states, nationally, or in other countries. A limitation with retrospective chart is the reliance on

Scholarly Project Final Report

charting for determining accurate drug use and SAB details.

There are many prospects for future studies based off the findings of this study. It would be helpful to find ways to improve antibiotic completion and decrease patient-directed discharges in PWID in order to improve recurrence and readmission rates. Our study showed that MOUD prescription at discharge improved antibiotic completion rates, but there are other potential avenues including researching treatment options for stimulant use disorder as well as long-acting injectable antibiotics such as dalbavancin/oritavancin, quality improvement projects focusing on increasing MOUD prescribing while inpatient and at discharge, care models that pair outpatient parenteral antibiotic therapy with outpatient treatment for SUD, as well as the role of an oral antibiotic contingency plan for patient-directed discharges. Emerging studies are showing growing evidence that a transition to oral antibiotics in SAB can be safe, effective, and reduce 90-day readmission in PWIDs who leave the hospital as a PDD^{29,34-36}. Additionally, there is a call for experts in both infectious diseases and addiction medicine and broad expansion of addiction medicine services at hospitals that manage SAB³⁷.

Conclusions

Overall, persons who inject drugs experience a different bacteremia and outcome profile than persons who do not inject drugs despite receiving comparable standards of care for SAB. Understanding the differences in groups can help inform the provider's clinical practice. With lower therapy completion rates, higher PDD, and social barriers that impede clinical outcomes in PWID, unique approaches are needed to improve outcomes. Initiating medication for opioid use disorder to treat the underlying addiction is one important intervention available to clinicians.

References

1. Bassetti S, Battegay M. Staphylococcus aureus infections in injection drug users: risk factors and prevention strategies. *Infection*. Jun 2004;32(3):163-9. doi:10.1007/s15010-004-3106-0
2. Scheidegger C, Zimmerli W. Infectious complications in drug addicts: seven-year review of 269 hospitalized narcotics abusers in Switzerland. *Rev Infect Dis*. May-Jun 1989;11(3):486-93. doi:10.1093/clinids/11.3.486
3. Coyle JR, Freeland M, Eckel ST, Hart AL. Trends in Morbidity, Mortality, and Cost of Hospitalizations Associated With Infectious Disease Sequelae of the Opioid Epidemic. *J Infect Dis*. Sep 2 2020;222(Suppl 5):S451-S457. doi:10.1093/infdis/jiaa012
4. Capizzi J, Leahy J, Wheelock H, et al. Population-based trends in hospitalizations due to injection drug use-related serious bacterial infections, Oregon, 2008 to 2018. *PLoS One*. 2020;15(11):e0242165. doi:10.1371/journal.pone.0242165
5. 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*. Oct 23 2020;71(7):e37-e44. doi:10.1093/cid/ciaa008
6. Ronan MV, Herzig SJ. Hospitalizations Related To Opioid Abuse/Dependence And Associated Serious Infections Increased Sharply, 2002-12. *Health Aff (Millwood)*. May 1 2016;35(5):832-7. doi:10.1377/hlthaff.2015.1424
7. Gordon RJ, Lowy FD. Bacterial Infections in Drug Users. *New England Journal of Medicine*. 2005;353(18):1945-1954. doi:10.1056/NEJMra042823
8. van Hal SJ, Jensen SO, Vaska VL, Espedido BA, Paterson DL, Gosbell IB. Predictors of mortality in Staphylococcus aureus Bacteremia. *Clin Microbiol Rev*. Apr 2012;25(2):362-86. doi:10.1128/CMR.05022-11

Scholarly Project Final Report

9. Serota DP, Niehaus ED, Schechter MC, et al. Disparity in Quality of Infectious Disease vs Addiction Care Among Patients With Injection Drug Use-Associated *Staphylococcus aureus* Bacteremia. *Open Forum Infect Dis*. Jul 2019;6(7):ofz289. doi:10.1093/ofid/ofz289
10. Acheson LS, Siefried KJ, Clifford B, et al. One-third of people who inject drugs are at risk of incomplete treatment for *Staphylococcus aureus* bacteraemia: a retrospective medical record review. *Int J Infect Dis*. Nov 2021;112:63-65. doi:10.1016/j.ijid.2021.09.012
11. Dahlman D, Berge J, Nilsson AC, Kral AH, Bjorkman P, Hakansson AC. Opioid and amphetamine dependence is associated with methicillin-resistant *Staphylococcus aureus* (MRSA): An epidemiological register study with 73,201 Swedish in- and outpatients 1997-2013. *Infect Dis (Lond)*. Feb 2017;49(2):120-127. doi:10.1080/23744235.2016.1237038
12. Jackson KA BM, Brooks JT, et al. Invasive Methicillin-Resistant *Staphylococcus aureus* Infections Among Persons Who Inject Drugs - Six Sites, 2005-2016. *MMWR Morb Mortal Wkly Rep*. June 8 2018 2018;67(22):625-628.
13. Ti L, Ti L. Leaving the Hospital Against Medical Advice Among People Who Use Illicit Drugs: A Systematic Review. *Am J Public Health*. Dec 2015;105(12):e53-9. doi:10.2105/AJPH.2015.302885
14. 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*. Mar 2014;105:59-66. doi:10.1016/j.socscimed.2014.01.010
15. Kim JH, Fine DR, Li L, et al. Disparities in United States hospitalizations for serious infections in patients with and without opioid use disorder: A nationwide observational study. *PLoS Med*. Aug 2020;17(8):e1003247. doi:10.1371/journal.pmed.1003247
16. Appa A, Adamo M, Le S, et al. Comparative 1-Year Outcomes of Invasive *Staphylococcus aureus* Infections Among Persons With and Without Drug Use: An Observational Cohort Study. *Clin Infect Dis*. Jan 29 2022;74(2):263-270. doi:10.1093/cid/ciab367
17. Holland TL, Arnold C, Fowler VG, Jr. Clinical management of *Staphylococcus aureus* bacteremia: a review. *JAMA*. Oct 1 2014;312(13):1330-41. doi:10.1001/jama.2014.9743
18. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis*. Feb 1 2011;52(3):e18-55. doi:10.1093/cid/ciq146
19. Jung N, Rieg S. Essentials in the management of *S. aureus* bloodstream infection. *Infection*. Aug 2018;46(4):441-442. doi:10.1007/s15010-018-1130-8
20. Bassetti M, Peghin M, Trecarichi EM, et al. Characteristics of *Staphylococcus aureus* Bacteraemia and Predictors of Early and Late Mortality. *PLoS One*. 2017;12(2):e0170236. doi:10.1371/journal.pone.0170236
21. Honda H, Krauss MJ, Jones JC, Olsen MA, Warren DK. The value of infectious diseases consultation in *Staphylococcus aureus* bacteremia. *Am J Med*. Jul 2010;123(7):631-7. doi:10.1016/j.amjmed.2010.01.015
22. Goto M, Schweizer ML, Vaughan-Sarrazin MS, et al. Association of Evidence-Based Care Processes With Mortality in *Staphylococcus aureus* Bacteremia at Veterans Health Administration Hospitals, 2003-2014. *JAMA Intern Med*. Oct 1 2017;177(10):1489-1497. doi:10.1001/jamainternmed.2017.3958
23. Ruotsalainen E, Sammalkorpi K, Laine J, et al. Clinical manifestations and outcome in *Staphylococcus aureus* endocarditis among injection drug users and nonaddicts: a prospective study of 74 patients. *BMC Infect Dis*. Sep 11 2006;6:137. doi:10.1186/1471-2334-6-137

Scholarly Project Final Report

24. Parikh MP, Octaria R, Kainer MA. Methicillin-Resistant Staphylococcus aureus Bloodstream Infections and Injection Drug Use, Tennessee, USA, 2015-2017. *Emerg Infect Dis*. Mar 2020;26(3)doi:10.3201/eid2603.191408
25. Cosgrove SE SG, Perencevich EN, Schwaber MJ, Karchmer AW,, Y. C. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible Staphylococcus aureus bacteremia: a meta-analysis. *Clin Infect Dis*. 2003;38:331-5
26. Inagaki K, Lucar J, Blackshear C, Hobbs CV. Methicillin-susceptible and Methicillin-resistant Staphylococcus aureus Bacteremia: Nationwide Estimates of 30-Day Readmission, In-hospital Mortality, Length of Stay, and Cost in the United States. *Clin Infect Dis*. Nov 27 2019;69(12):2112-2118. doi:10.1093/cid/ciz123
27. Wagner K, Zhong Y, Teshale E, et al. Hepatitis C virus infection and polysubstance use among young adult people who inject drugs in a rural county of New Mexico. *Drug Alcohol Depend*. Mar 1 2021;220:108527. doi:10.1016/j.drugalcdep.2021.108527
28. 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*. Sep 2 2020;222(Suppl 5):S513-S520. doi:10.1093/infdis/jiz516
29. 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*. Dec 17 2020;71(10):e650-e656. doi:10.1093/cid/ciaa365
30. Englander H, Dobbertin K, Lind BK, et al. Inpatient Addiction Medicine Consultation and Post-Hospital Substance Use Disorder Treatment Engagement: a Propensity-Matched Analysis. *J Gen Intern Med*. Dec 2019;34(12):2796-2803. doi:10.1007/s11606-019-05251-9
31. Saitz R. Treatment for Opioid Addiction Must Be Offered in General Hospitals: But How? *J Addict Med*. Mar/Apr 2019;13(2):83-84. doi:10.1097/ADM.0000000000000501
32. Serota DP, Bartholomew TS, Tookes HE. Evaluating Differences in Opioid and Stimulant Use-associated Infectious Disease Hospitalizations in Florida, 2016-2017. *Clin Infect Dis*. Oct 5 2021;73(7):e1649-e1657. doi:10.1093/cid/ciaa1278
33. Simon R, Snow R, Wakeman S. Understanding why patients with substance use disorders leave the hospital against medical advice: A qualitative study. *Subst Abus*. 2020;41(4):519-525. doi:10.1080/08897077.2019.1671942
34. Kouijzer IJE, van Leerdam EJ, Gompelman M, et al. Intravenous to Oral Switch in Complicated Staphylococcus aureus Bacteremia Without Endovascular Infection: A Retrospective Single-Center Cohort Study. *Clin Infect Dis*. Sep 7 2021;73(5):895-898. doi:10.1093/cid/ciab156
35. Perez-Rodriguez MT, Sousa A, Moreno-Flores A, et al. The benefits and safety of oral sequential antibiotic therapy in non-complicated and complicated Staphylococcus aureus bacteremia. *Int J Infect Dis*. Jan 2021;102:554-560. doi:10.1016/j.ijid.2020.10.097
36. Martinez AE, Scheidegger C, Battig V, Erb S. Oral antibiotic therapy in people who inject drugs (PWID) with bacteraemia. *Swiss Med Wkly*. Jun 1 2020;150:w20259. doi:10.4414/smw.2020.20259
37. Serota DP, Barocas JA, Springer SA. Infectious Complications of Addiction: A Call for a New Subspecialty Within Infectious Diseases. *Clin Infect Dis*. Feb 14 2020;70(5):968-972. doi:10.1093/cid/ciz804

Scholarly Project Final Report

Figures and Tables

Table 1. *Staphylococcus aureus* Bacteremia: Comparison of Demographics, Comorbidities, and Infection Characteristics among Patients With and Without Intravenous Drug Use

	Overall (n=248)	PWID (n=70, 28.2%)	Non-PWID (n=178, 71.8%)	PValue
Patient Demographics and Characteristics				
Age, median (range), years	52 (19-97)	37 (21-65)	57 (19-97)	<0.0001
Male sex, No. (%)	165 (66.5)	43 (61.4)	122 (68.5)	0.3
Race, No. (%)				0.72
White	213 (85.9)	61 (87.1)	152 (85.4)	
Other	35 (14.1)	9 (12.9)	26 (14.6)	
Experiencing Homelessness, No. (%) ^a	36 (14.7)	29 (43.3)	7 (3.9)	<0.0001
Comorbidities, No. (%)				
Hepatitis C ^b	43 (7.8)	34 (53.1)	9 (7.8)	<0.0001
HIV ^c	8 (4.4)	4 (6.3)	4 (3.4)	0.38
Diabetes	63 (25.4)	7 (10.0)	56 (31.5)	<0.001
Hemodialysis	16 (6.5)	0 (0.0)	16 (9.0)	0.01
Malignancy	42 (16.9)	1 (1.4)	41 (23.0)	<0.001
Bacteremia Characteristics				
Organism, No. (%)				
MSSA	152 (61.3)	31 (44.3)	121 (68.0)	<0.001
MRSA	96 (38.7)	39 (55.7)	57 (32.0)	<0.001
Polymicrobial ^d	27 (11.0)	7 (10.0)	20 (11.4)	0.64
Duration of Bacteremia, median (IQR), days ^e	3.0 (0.3-26.9)	4.3 (0.9-19.7)	2.7 (0.3-26.9)	0.03
Complications, No. (%)				
Definite and Possible				
Endocarditis ^f	70 (28.3)	33 (47.1)	37 (20.9)	<0.001
Spinal Epidural Abscess/Osteomyelitis ^f	43 (17.4)	18 (25.7)	25 (14.1)	0.03
SSTI ^g	45 (18.4)	19 (27.5)	26 (14.8)	0.02
DVT/SVT ^h	42 (17.0)	12 (17.1)	30 (16.9)	0.971

Abbreviations: PWID, persons who inject drugs; HIV, human immunodeficiency virus; MSSA, methicillin-susceptible *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; SSTI, Skin and soft tissue infection; DVT, deep vein thrombosis; SVT, superficial vein thrombosis. ^a Where homelessness is known, PWID (n=67), overall (n=245), Fisher's exact used ^b Where hepatitis C virus is known, PWID (n=64), non-PWID (n=115), overall (n=179) ^c Where HIV status is known, PWID (n=64), non-PWID (n=116), overall (n=180) ^d Where polymicrobial data is known, non-PWID (n=176), overall (n=246) ^e Where duration is known, non-PWID (n=176), overall (n=246) ^f Where complication status is known, non-PWID (n=177), overall (n= 247). Definite and possible endocarditis based on modified Duke criteria (excluding fever and injection drug use as minor criteria). ^g Where SSTI status is known. PWID (n=69), non-PWID (n=176), overall (n=245) ^h Where DVT/status is known. Non-PWID (n=177), overall (n=247)

Scholarly Project Final Report

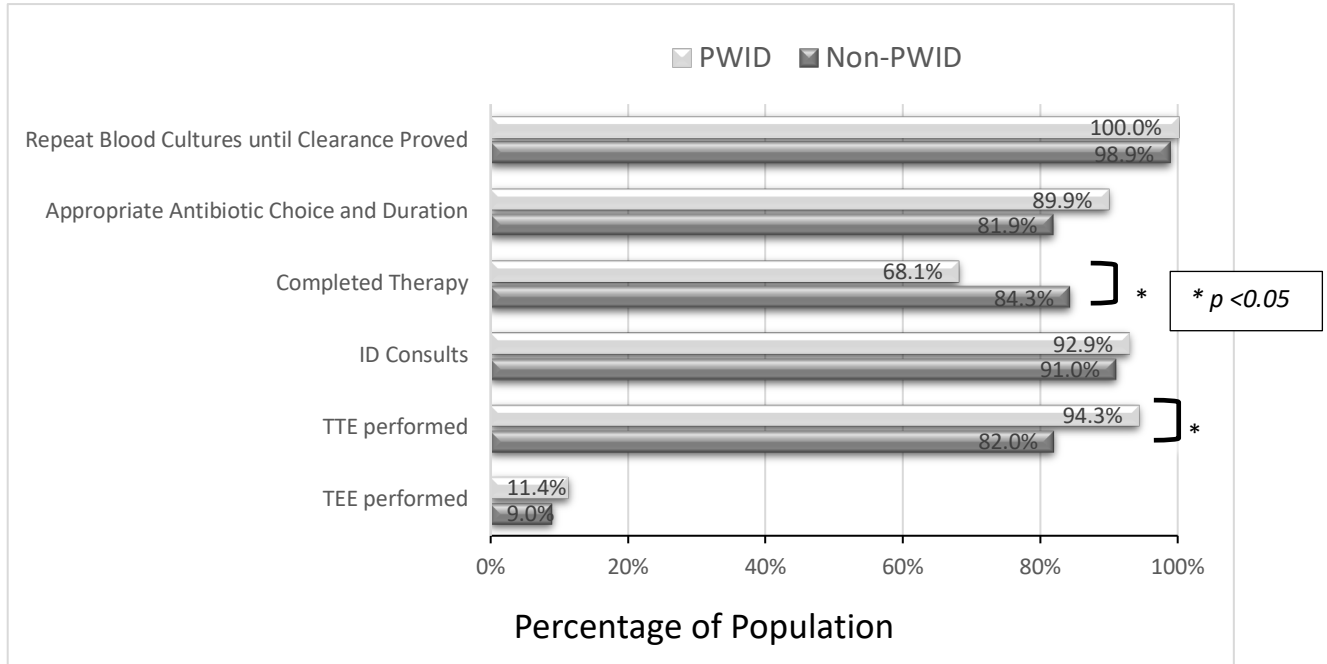
Table 2. Characteristics of Substance Use and Management in PWID Admitted for SAB

Of PWID (n=70):	No. (%)
Opioid Use	59 (84.3)
Opioid Use Disorder ^a	53 (82.8)
Methamphetamine Use	59 (84.3)
Stimulant Use Disorder ^a	45 (78.9)
Opioid and Stimulant Use	50 (71.4)
Active Use ^b	61 (88.4)
Addiction Team Consult	30 (42.9)
Of those with OUD (n=53):	
Active Use	48 (90.6)
DSM-5 Severity Score	
Severe	48 (90.6)
Moderate	3 (5.7)
Unknown	2 (3.8)
Stimulant Use	46 (86.8)
Addiction Team Consult	26 (49.1)
Received Inpatient MOUD	39 (73.6)
Initiated Inpatient	34 (64.2)
Continued from pre-admission	5 (9.4)
Type of MOUD Received While Inpatient	
Methadone	25 (47.2)
Buprenorphine/Naloxone	9 (17.0)
Buprenorphine	2 (3.8)
Methadone to Buprenorphine/Naloxone	3 (5.7)
Patient Declined When Offered MOUD	9 (17.0)
MOUD Prescription at Discharge	16 (30.2)
MOUD Prescribed at Discharge	
Suboxone	9 (17.0)
Methadone	7 (13.2)
MOUD Referral with Discharge	23 (43.4)

Abbreviations: PWID, persons who inject drugs; SAB, *Staphylococcus aureus* bacteremia; OUD, opioid use disorder; DSM-5, Diagnostic and Statistical Manual of Mental Disorders; MOUD, medications for opioid use disorder ^a Where substance use is known in PWID: opioid use disorder (n=64), stimulant use disorder (n=57) ^b Active use defined as substance use in the last month. Where active use is known in PWID (n=69)

Scholarly Project Final Report

Figure 1. Adherence to SAB Standards of Care in PWID vs. Non-PWID



Abbreviations: PWID, persons who inject drugs; ID, infectious diseases; TTE, transthoracic echocardiogram; TEE, transesophageal echocardiogram

Table 3. Comparison of Clinical Outcomes of SAB among Patients With and Without Intravenous Drug Use

	Overall (n=248)	PWID (n=70, 28.2%)	Non-PWID (n=178, 71.8%)	PValue
Hospitalization Duration, median (range), days	15 (3-118)	21.5 (3-118)	14 (3-90)	<0.001
PDD, No. (%)	20 (8.1)	18 (25.7)	2 (1.1)	<0.001
Inpatient mortality, No. (%)	20 (8.1)	3 (4.3)	17 (9.6)	0.17
SAB Recurrence within 90 days ^a	18 (8.1)	8 (12.1)	10 (6.4)	0.15
Readmitted within 90 days ^b , No. (%)	86 (41.0)	31 (47.0)	55 (38.2)	0.23
90-day Mortality ^c , No. (%)	37 (15.0)	4 (5.7)	33 (18.6)	<0.01

Abbreviations: SAB, *Staphylococcus aureus* bacteremia; PWID, persons who inject drugs; PDD, Patient directed discharge also known as leaving against medical advice “AMA” ^a Recurrence defined as a positive blood culture after ≥ 72 hours of negative blood cultures with same organism. Excluding patients who died during index hospitalization and cases with unknown 90-day recurrence data. Overall (n=222), PWID (n=66), non-PWID (n=156) ^b Excluding patients who died during index hospitalization or within 90 days. Overall (n=210), PWID (n=66), non-PWID (n=144) ^c Where death within 90 days is known. Overall (n=247), non-PWID (n=177). Fisher’s exact test used.

Scholarly Project Final Report

Table 4. Multivariate Analysis of Clinical Outcomes for Overall Cohort and PWID

	Variable	Odds Ratio	95% CI	PValue
<u>Did Not Complete</u>				
<u>Antibiotic Course</u>				
Overall Group	IV Drug Use	2.52	1.28-4.96	0.008
	Treatment Duration >2 weeks (vs. <2 weeks)	4.29	1.42-12.98	0.01
	ID Consult	0.15	0.05-0.51	0.002
PWID	MAT Prescription at Discharge	0.04	0.004-0.40	0.006
	Opioid Use Disorder	18.38	1.84-183.92	0.01
	Mood Disorder	0.26	0.07-1.02	0.05
<u>Patient Directed Discharge</u>				
Overall Group	IV Drug Use	19.22	4.09-90.28	0.0002
	Age	0.96	0.92-1.01	0.1008
PWID	Hepatitis C Virus	4.55	1.30-15.96	0.02

Abbreviations: PWID, persons who inject drugs; CI, confidence interval; IV, intravenous; ID, infectious diseases; MAT, medication-assisted treatment