A Novel Program to Provide Drug Recovery Assistance and Outpatient Parenteral Antibiotic Therapy in People Who Inject Drugs

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ABSTRACT

Background

Safe hospital discharge on parenteral antibiotic therapy is challenging for people who inject drugs (PWID) admitted with serious bacterial infections (SBI). We describe a Comprehensive Care of Drug Addiction and Infection (CCDAI) program involving a partnership between Intermountain Healthcare hospitals and a detoxification facility (DF) to provide simultaneous drug recovery assistance and parenteral antibiotic therapy (DRA-OPAT).

Methods

The CCDAI program was evaluated using a pre-post study design. We compared outcomes in PWID hospitalized with SBI during a 1-year post-implementation period (2018) with similar patients from a historical control period (2017), identified by propensity modeling and manual review.

Results

Eighty-seven patients were candidates for the CCDAI program in the implementation period. 35 participants (40.2%) enrolled in DRA-OPAT and discharged to the DF; 16 (45.7%) completed the full OPAT duration. Fifty-one patients with similar characteristics were identified as a pre-implementation control group. Median length of stay (LOS) was reduced from 22.9 days (IQI 9.8-42.7) to 10.6 days (IQI 6-17.4) after program implementation, p<0.0001. Total median cost decreased from $39,220.90 (IQI $23,300.71-$82,506.66) pre-implementation vs $27,592.39 (IQI $18,509.45-$48,369.11) post-implementation, p<0.0001. 90-day readmission rates were similar (23.5% vs 24.1%), p=0.8. At 1-year follow-up, all-
cause mortality was 7.1% in the pre-implementation group vs 1.2% post-implementation, p=0.06.

Conclusion

Partnerships between hospitals and community resources hold promise for providing resource efficient OPAT and drug recovery assistance. We observed significant reductions in length of stay and cost without increases in readmission rates; 1-year mortality may have been improved. Further study is needed to optimize benefits of the program.

Key Words: OPAT; PWID; Substance Abuse; antimicrobial stewardship
Introduction

The opioid epidemic has caused a significant increase in hospitalizations for treatment of serious bacterial infections (SBI) in people who inject drugs (PWID)\(^1\)-\(^3\). These infections often require prolonged treatment with parenteral antibiotic therapy via a peripherally inserted central catheter (PICC). Outpatient parenteral antibiotic therapy (OPAT) is a safe and cost-effective method to treat patients outside of the inpatient setting. Treatment is usually received at home via home healthcare or at an infusion center. Historically, PWID have not been considered safe candidates for OPAT due to concerns of line manipulation for illicit drug use, noncompliance, complicated social situations\(^4\), and higher risk of failure\(^5\). Stemming from these concerns it has become common practice to require PWID with serious infections to remain hospitalized to receive standard of care durations of intravenous (IV) antibiotic treatment\(^4\). These prolonged hospitalizations, sometimes up to 6 weeks can cause significant financial burden on the hospital and inefficient use of acute care hospital resources\(^1\). Often the focus during the hospitalization is treatment of the infection and as a result the underlying substance abuse disorder is not being adequately addressed.

Patients who use drugs admitted to the hospital for invasive *Staphylococcus aureus* infection were found to have lower antibiotic completion rates and increased readmission rates due to recurrent or persistent infection\(^6\). Collaboration between hospital systems and community partners focused on substance use disorder may provide PWID with SBI requiring parenteral antibiotics upon discharge a safe environment where they can receive OPAT while having the opportunity to engage in addiction-related treatment.

This study aimed to evaluate a new program that provided Comprehensive Care of Drug Addiction and Infection (CCDAI) to hospitalized PWID with SBI and facilitated transition to
a nonprofit residential detox facility (DF) where they received supervised self-administered outpatient parenteral antibiotic therapy and drug recovery assistance (DRA-OPAT).

Methods

_Inpatient Comprehensive Care of Drug Addiction and Infection Team and Patients:_ From January 2018-December 2018 a multidisciplinary Comprehensive Care of Drug Addiction and Infection (CCDAI) team made up of an infectious diseases (ID) physician, hospitalist, psychiatrist, case management, infectious diseases pharmacist, home healthcare (HH) nurse, as well as a liaison from the DF met weekly to review patients with SBI and concomitant substance use disorder (SUD) hospitalized at four Salt Lake County Intermountain Healthcare hospitals. Hospitalists, case managers, ID physicians and pharmacists referred patients to the multidisciplinary team based on clinical concern for SUD and a current diagnosis of SBI likely requiring treatment with prolonged IV antibiotics. These patients were evaluated by members of the CCDAI team during their inpatient admission. Psychiatry consultation and medications for opioid use disorder (MOUD) were provided to patients when appropriate. Amenable patients requiring treatment with outpatient IV antibiotics who met eligibility criteria were enrolled in the DRA-OPAT part of the program and were transitioned to the DF. Enrollment eligibility criteria included: mandatory inpatient ID consultation, medically stable for discharge, stable mental illness, independent with activities of daily living (ADLs), physical and cognitive ability to self-infuse IV antibiotics, tapering regimen if opioids were needed for pain, and an IV antibiotic regimen that can infuse in < 20 minutes or delivered in a 24 hour continuous infusion. Hospitalized patients who met eligibility criteria for DRA-OPAT but declined enrollment in the program were discharged from the hospital on an oral antibiotic salvage regimen determined by the treatment team if disposition to a skilled nursing facility was not feasible.
Drug Recovery Assistance and Community Partnership: The nonprofit residential DF located in Salt Lake City, Utah provides the community with 83 male beds and a separate 30-bed women’s facility for detoxification and withdrawal management services for up to 14-day stays. The hospital system subsidized the DF with a fixed contractual rate to provide 5 beds at each facility in a private dorm room separate from the detox beds, for patients enrolled in the DRA-OPAT program. The patients received three meals daily and could remain at the facility for the duration of their OPAT. Case management was provided to the patients during their stay at the DF and assisted with transitioning patients to residential or outpatient treatment programs upon completion of OPAT. Patients were encouraged to attend 12-Step meetings, Seeking Safety and peer support groups. The DF partnered with a community nonprofit opioid treatment program that provided clinical assessment and treatment plans which included MOUD in addition to behavior counseling. Random urine drug screens were performed by the DF if drug use was suspected. HH pharmacy provided IV antibiotics and the patients were taught by HH nurses to self-administer their IV antibiotics. HH nurses made weekly and as needed visits to the patients during their stay at the DF. Physical therapy and wound care were provided by HH if needed. Patients infused their antibiotic in the medication room while being monitored by non-medical facility staff. The DF provided transportation to medical appointments and all patients received follow up care by an ID physician. Patients who enrolled in the DRA-OPAT but either elected to leave the program prior to completing their prescribed course of IV antibiotics or were dismissed from the DF as a result of a positive random urine drug screen or nonadherence to the facility behavior contract were transitioned to oral antibiotic therapy. The PICC line was removed by a HH nurse or the patient was transported to the hospital emergency department for PICC removal. Completion of therapy was defined as receiving equal to or greater than the days of OPAT prescribed by the inpatient ID consultation team.
Statistical Analysis

We used a pre-/post- study design to evaluate the effect of implementation of the CCDAI program. During the post-implementation period (January-December 2018), all PWID hospitalized for SBI requiring IV antibiotics who were referred to the CCDAI team for evaluation and were recorded in a registry (RedCap, Nashville TN). We will refer to this group of inpatients as program Candidates, effectively an intention-to-treat (ITT) population. From this group, patients who were actually discharged to the community partner DF and enrolled in the DRA-OPAT part of the program will be referred to as Participants (effectively a per-protocol, or rather per-program (PER-PROGRAM) cohort).

In order to identify a historical control with comparable clinical characteristics, we employed a hybrid approach consisting of initial propensity-score cohort discovery and subsequent manual review. The rationale for this mixed approach was that although there are many billing codes for substance abuse, there is no billing code or other electronic signature that accurately identifies patients who inject drugs. Hence this key data limitation to propensity-matching was identified a priori and addressed by manual review. In order to develop the propensity score, we first identified all discharge diagnosis codes (International Classification of Diseases, 10th revision) associated with (1) substance abuse and (2) SBI (See Supplemental data). We then queried all admissions to study hospitals during the program implementation period to identify patients with (1) at least one code identifying drug abuse and (2) one code identifying SBI (see Figure 1). We confirmed that all program candidates from the ITT population were found within this larger pool. We then excluded patients who would not have been evaluable for the program, including: patients who expired in the hospital because they were never stable enough to consider disposition, patients discharged to hospice, those discharged to behavioral health units, and those who left AMA before an ID consult note was
entered, with the rationale that these patients would not have been in the hospital long enough to have been evaluated. We also excluded patients readmitted after a recently diagnosed SBI.

Once this larger cohort of PWID with SBI was identified from the post-implementation period, we then developed a propensity score model. This was done by developing a logistic regression model with all actual program candidates as the dependent variable. An optimal model was fitted after exploring all available covariates for their ability to discriminate program candidates from patients who were not. Validation of model discrimination was confirmed via the area under the receiver operator characteristic curve (AUROC) and Hosmer-Lemeshow goodness of fit tests.

Once an adequate propensity model was developed, we then turned our attention to identifying a historical control. First, we followed identical methodology as described above to search for all patients during a one-year pre-implementation period (Jan-Dec 2017) who had both (1) a discharge diagnosis for substance abuse and (2) discharge diagnose(es) for SBI. We then applied the propensity score to this cohort from the pre-implementation period to stratify patients based on likelihood that they would have been program candidates had the program existed. We selected a predicted probability cutoff that captured all the known program candidates in the post implementation group and applied this to the pre-implementation group to identify patients at or above that predicted probability.

Study investigators then manually reviewed the electronic health record (EHR) for these cases to confirm that they had documentation of injection drug abuse. This final cohort became the pre-implementation group cohort of likely program candidates. Balance of characteristics between the pre- and post-implementation intention-to-treat groups was confirmed using Chi square, Fisher’s exact, or Mann-Whitney U tests, as appropriate (see Table 1). These tests were two-tailed with statistical significance at p <0.05; we adjusted
patient characteristics and outcomes analyses for a 5% false discovery rate (FDR) using the Benjamini-Hochberg method\(^7\).

From within this pre-implementation group of inpatients who likely would have been program candidates (historical ITT cohort), we sought to identify the patients who would have enrolled in the outpatient part of the program and actually been DRA-OPAT participants (per-program group) at the community partner program facility, had it existed. We recognized \textit{a priori} that propensity-matching would not be possible because the many factors that lead to a patient being approved by the evaluation committee and actually matriculating into the program are varied, largely psycho-social and not available in the EHR. To address this, we assigned the actual sitting members of the program evaluation committee to independently review the EHR record, including clinical characteristics and social work narrative notes, and adjudicate whether the patient was likely to have been discharged to participate in the program or not. All cases were independently reviewed by two different committee members, and the inter-rater agreement (kappa) was calculated. An independent committee member served as a blinded tiebreaker for cases in which the two reviewers differed. In this way, we identified a pre-implementation per-program control group consisting of likely DRA-OPAT program participants. Similarly, we compared clinical and demographic characteristics between the pre- and post-implementation groups using appropriate statistical tests as described above (see Table 2). These tests were also two-tailed with statistical significance at \(p <0.05\) and adjusted for a 5% FDR.

The pre-specified co-primary analyses were to compare pre- and post-implementation length of hospital stay and total cost in the program candidates (ITT) group. For cost data, we used total inpatient costs and the cost to maintain the community partner beds but did not include antibiotic costs. Secondary analyses included total cost and length of stay (LOS) in the participants (per-program) group, and 30- and 90-day all-cause readmission, 30-day- and 1-
year all-cause mortality in both ITT and per-program groups. Mortality data was obtained from the Utah Population Database (UPDB), which permits ascertainment of that outcome independent of the limitations of the hospital network or medical record. Finally, we planned a post-hoc sensitivity analysis using a multiple linear regression for LOS and total cost in the ITT and per-program groups to control for any remaining imbalanced covariates in the pre- and post-implementation cohorts. The study was approved by the Intermountain Healthcare Institutional Review Board. All statistical analyses were performed using SPSS version 25 (IBM Corporation, Armonk, NY).

Results

Cohort Discovery

During cohort discovery, 855 patients were identified with discharge diagnoses for both a SBI and substance abuse during the post-implementation period, and 454 patients were identified during the pre-implementation period (See Figure 1). The differences in sample sizes was reflective of a new electronic health record which was being implemented during the pre-implementation period. The variables included in the final logistic regression model developed as a propensity score for identifying the historical cohort are listed in supplementary Table 1. Discrimination (AUROC .949) and classification (93.2% accuracy) of the model was excel ent. Kappa agreement was 0.6 for determining likely historical program participants.

Clinical Characteristics and Outcomes

During the post-implementation period, 87 hospitalized patients were identified as CCDAI program candidates (ITT population). 35 patients (40.2%) were ultimately enrolled and discharged to the DRA-OPAT facility (per-program group) (Figure 1); of these 16 (45.7%)


completed the full OPAT duration at the center. In the pre-implementation group, 51 patients were identified as likely to have been candidates had the program existed. Of these, the program evaluation committee determined that 31 (60.8%) would likely have been DRA-OPAT participants. Patient characteristics for the program candidates (ITT) group by pre- and post-implementation periods is displayed in Table 1. Patients in both groups were well-balanced in terms of demographics, patterns of drug abuse, type of infection and surgical intervention (see Table 1). There were more patients with congestive heart failure and chronic pulmonary disease in the historical control group and more patients with spinal infections in the post-implementation group; however, these differences were not statistically significant after adjusting for FDR.

Median LOS was reduced from 22.9 days (IQI 9.8-42.7) to 10.6 days (IQI 6-17.4) after program implementation, p<0.0001 (Table 1). Total cost per patient was also decreased from $39,220.90 (IQI $23,300.71-$82,506.66) pre-implementation to $27,592.39 (IQI $18509.45-48369.11) post-implementation, p<0.0001 (supplementary Figure 1). More patients completed the duration and route of antibiotic course as originally prescribed in the pre-implementation group (66.7% vs 18.4%); this difference largely reflects IV-to-oral transitions to complete therapy in patients who declined participation in the program and those who decided to leave the community-partner facility prior to the originally anticipated stop date. 30-day readmission was numerically more frequent after program implementation (7.8% vs 12.6%, p=0.09) but there was no difference in 90-day readmission (23.5% vs 24.1%), p=0.8. At 1-year follow-up, all-cause mortality was 7.1% in the pre-implementation group vs 1.2%, p=0.06. Pre-planned sensitivity analyses adjusting for residual imbalanced factors (CHF, chronic pulmonary disease and spinal infection) confirmed significant reductions in LOS (unstandardized β coefficient -12.7 days (95% confidence interval -17.7 to -7.6, p<0.0001), and total cost β coefficient $-19,925.82 (95% CI -31,194.50 to -8,657.15, p=0.001).
Patient characteristics were similar between pre- and post-implementation groups in the per-protocol cohort of DRA-OPAT participants (see Table 2). In this sub-group, median LOS was 35.1 days (IQI 16.7-46.8) pre- vs 12.1 days (IQI 8.9-17.9) post-implementation, p<0.0001 (Table 2). Total inpatient costs were $68,748.20 (IQI $34,485.35-$112,712.08) pre- vs $33,231.88 (IQI $24,170.49-$46,670.35) post-implementation, p<0.0001. In sensitivity analyses, reductions in LOS (unstandardized β coefficient -21.3 days (95% confidence interval -28.4 to -14.1, p<0.0001), and total cost, β coefficient $-36,285.50 (95% CI -53,028.29 to -19,542.70, p<0.0001) remained significant.

Of the 35 DRA-OPAT participants, 16 completed the originally recommended duration of therapy at the DF, and 19 did not (Table 3). Numerically stimulant use and polysubstance use were more common among DRA-OPAT participants who did not complete treatment. Two patients absconded with their PICC line and two patients violated the program behavioral contract and had positive urine drugs of abuse screens during their stay. Two patients required readmission due antibiotic-related adverse events. The median LOS at the DF for those that completed was 24 days (IQI 19.5-38), compared to 4 days (IQI 2-9) for those who did not. Factors that correlated with successful completion of therapy included active MOUD (OR 17.0 95% CI 2.1-136, p=0.008) and homelessness (OR 8.1, CI 1.2-53.7, p=0.03).

Substance used (opioid vs methamphetamine), race, and length of hospital stay prior to discharge may also contribute but we had inadequate sample size to confirm these observations.

Discussion

This study describes outcomes data for a new program that utilized a multidisciplinary approach to inpatient management of drug addiction and infection as well as a unique partnership with a community nonprofit residential DF that provided PWID with concomitant...
SBI to receive DRA-OPAT. Our results demonstrate significant decrease in hospital LOS and subsequent inpatient costs when these complex patients are no longer kept in the hospital for the duration of their prescribed IV antibiotic course. Following initiation of this new program, mortality and readmission rates did not increase despite lower IV antibiotic treatment completion rates. Benefits of shortening the inpatient LOS for this patient population once they become medically stable allows for earlier engagement in outpatient addiction treatment as well as access to outpatient resources focused on psychological, social, and environmental contributors to addiction. These types of resources are not readily available to patients while they remain hospitalized. Prolonged inpatient stays solely for receipt of IV antibiotics are no longer sustainable for many hospitals due to significant expense as well as critical nursing and bed shortages.

Prior published studies have described nurse administered OPAT to PWID in a respite facility, residential addiction treatment facility, and homelike alternative to a hospital. Our program differed from these as the OPAT site did not have any onsite medical staff. The patients that participated in the OPAT-DRA program were responsible for infusing their own antibiotics. The onsite staff observed and documented the antibiotic infusion, but they were not trained to assist. The 30-day re-admission rate for patients enrolled in the DRA-OPAT program was 11.4% which falls within the 6-25% range of OPAT readmission in the general population. Our study demonstrates that PWID are capable of safely self-administering their OPAT in a supervised setting without onsite medical staff. Residential addiction treatment programs are often unwilling to accept patients requiring OPAT due to their perception that these patients are higher medical acuity requiring more intense medical staffing. Hiring additional medically trained staffed is usually cost-prohibitive for these facilities. Our findings may compel more residential addiction treatment programs to admit
PWID requiring OPAT when enrolled in a structured OPAT program and closely followed by an ID specialist.

Recruitment of patients for these programs can be challenging. Englander et al. described a similar program that utilized a medically enhanced residential treatment model for integration of SUD and prolonged IV antibiotics. They had a low recruitment and retention rate and ultimately had to close the program after 6 months. Most patients who declined admission remained in the hospital or were discharged to a SNF. Our program enrolled 35 out of 85 (40.2%) of the CCDAI candidates into the DRA-OPAT part of the program. Some patients did not meet eligibility criteria due to inability to perform ADLs or infuse their own IV antibiotics. Others were not amenable to being discharged to the DF due to their prior experience at acute detox or the stigma associated with this facility. The DF had a strict policy prohibiting cell phones, internet access, unsupervised visitation, and leaving the center other than for medical or legal obligations. These restrictions deterred some patients from participating in the program and contributed to early attrition from the DRA-OPAT program.

Eligible patients for DRA-OPAT who declined transition to the DF were not given the choice to remain in the hospital and were discharged on oral salvage antibiotic therapy when transition to SNF was not feasible. This new policy may have contributed to higher recruitment than other programs described in the literature.

Assessment and initiation of MOUD by the hospitalist or psychiatry consult service during the inpatient stay was an integral part of our program. Treatment with MOUD was correlated with successful completion of antibiotic therapy in the DRA-OPAT participants and should be considered essential in any OPAT program for PWID. Our study found amphetamine and polysubstance use were more common in the DRA-OPAT participants who did not complete IV antibiotic treatment, although the impact of specific substance used on completion of therapy could not be determined due to inadequate sample size. Recent data suggests
methamphetamine use adversely affects MOUD receipt, retention and opioid abstinence in patients with opioid use disorder (OUD)\textsuperscript{14}.

Most of our DRA-OPAT participants who were treated with MOUD received methadone rather than buprenorphine due to cost and the DF’s established relationship with a community nonprofit opioid treatment program. Following completion of DRA-OPAT, arrangements were made for the participants to continue MOUD. CCDAI candidates who were initiated on MOUD inpatient but declined to participate in DRA-OPAT were also provided the opportunity to continue MOUD outpatient. Although most PWID hospitalized with SBI are not seeking addiction treatment, hospitalization creates an opportunity to engage patients in treatment and facilitate transition to an outpatient treatment program\textsuperscript{15,16}. Inpatient induction and linkage with outpatient buprenorphine compared to inpatient detoxification has been associated with lower illicit drug use at 6 months and increased entrance into outpatient buprenorphine treatment program\textsuperscript{17}. We hypothesize treatment with MOUD and/or referral to addiction treatment may have positively influenced the mortality and 90-day readmission rate of this group despite fewer patients completing standard of care IV antibiotic treatment for their infections\textsuperscript{18,19}.

\textit{Limitations}

This study was limited by retrospective study design and relatively small sample size. We acknowledge that although the historical control group was well-matched to the contemporary group, unmeasured differences may have been present. We were unable to accurately assess drug-rehabilitation/remission status, continuity of outpatient MOUD as well as engagement with other addiction treatment programs. This information would be useful for determining ultimate success of the program, as would larger sample size and longer follow-up period. The hospitals that participated in this study and the home health pharmacy and
nursing services were within the same healthcare corporation which allowed for access to a shared EHR, frequent communication, and close coordinated care that may not be generalizable. Our hospital system comprises a large percentage of admissions in the geographic area studied and includes the primary urban hospital as well. However, our data does not capture readmissions to hospitals outside of our system. Mortality data was obtained from the UPDB that is inclusive of all healthcare facilities in Utah. Finally, we recognize that this is only one of several novel therapeutic options now available to PWID requiring treatment of SBI. Future innovation should focus on enhancing the DRA component and studying other antibiotic options including early oral transition and novel depot glycopeptide formulations.

**Conclusion:**

In summary, this study demonstrates a successful treatment model that incorporates creative partnerships between hospitals and community resources to provide resource efficient OPAT and DRA. More research needs to be done on methods to improve program retention and identifying factors that influence which patients receive the greatest benefit from treatment in this program model.

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**Author Contributions:** Drs. Gelman and Webb had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Gelman, Webb, Stenehjem
Acquisition, analysis or interpretation of data: Grisel, Gelman, Webb, Foster, Tinker, Stenehjem

Drafting of the Manuscript: Gelman and Webb

Critical review of the manuscript for important intellectual content: All authors

Statistical Analysis: Webb

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**Table 1. Comparison of CCDAI Candidates by pre- and post-implementation period**

| Cohort                                      | Pre-Implementation (2017) | Post-Implementation (2018) | p=  |
|---------------------------------------------|---------------------------|-----------------------------|-----|
| Total N=                                    | 51                        | 87                          |     |
| Age, years (median, IQI)                    | 39 (35-47)                | 39 (30-51)                  | 0.55|
| Male, N (%)                                 | 29 (56.9)                 | 53 (60.9)                   | 0.72|
| Race, Non-White                             | 6 (9.8)                   | 12 (13.8)                   | 0.6 |
| Cocaine Use                                 | 2 (3.9)                   | 9 (10.3)                    | 0.21|
| Opioid Use                                  | 40 (78.4)                 | 65 (74.7)                   | 0.62|
| Polysubstance Use                           | 38 (74.5)                 | 55 (63.2)                   | 0.17|
| Stimulant Use                               | 26 (51.0)                 | 50 (57.5)                   | 0.46|
| Medication for opioid use disorder          | 31 (60.8)                 | 50 (57.5)                   | 0.7 |
| Homeless                                    | 24 (47.1)                 | 30 (34.5)                   | 0.14|
| HIV                                         | 1 (2.0)                   | 2 (2.3)                     | 1.0 |
| Hepatitis C                                 | 22 (43.1)                 | 26 (29.9)                   | 0.12|
| Charlson Comorbidity Index                  | 15.5 (6.0-43.5)           | 20 (12-36)                  | 0.56|
| Cerebrovascular Disease                     | 5 (9.8)                   | 8 (9.2)                     | 0.91|
| Congestive Heart Failure                    | 16 (31.4)                 | 13 (14.9)                   | 0.02†|
| Diabetes mellitus                           | 5 (9.8)                   | 11 (12.6)                   | 0.62|
| Hepatic Disease                             | 21 (41.2)                 | 35 (40.2)                   | 0.91|
| Chronic Pulmonary Disease                   | 27 (52.9)                 | 29 (33.3)                   | 0.02†|
| Kidney Disease                              | 8 (15.7)                  | 8 (9.2)                     | 0.25|
| Endocarditis                                | 20 (39.2)                 | 31 (35.6)                   | 0.67|
| Osteo-articular Infection                   | 16 (31.4)                 | 27 (31.0)                   | 0.97|
| Skin / Soft Tissue Infection                | 26 (51.0)                 | 47 (54.0)                   | 0.73|
| Vertebroabscess/Discitis/Osteomyelitis       | 7 (13.7)                  | 24 (27.6)                   | 0.06|
| Staphylococcus aureus Bacteremia            | 24 (47.1)                 | 38 (43.7)                   | 0.7 |
| Bone or Joint Debridement                   | 7 (13.7)                  | 19 (21.8)                   | 0.24|
| Cardiac Valve Replacement                   | 4 (7.8)                   | 3 (3.4)                     | 0.26|
| Soft Tissue Debridement                     | 16 (31.4)                 | 30 (34.5)                   | 0.71|
| Spinal Debridement                          | 8 (15.7)                  | 11 (12.6)                   | 0.6 |
| Infectious Disease Consult                  | 48 (94.1)                 | 79 (90.8)                   | 0.49|
| Completed Prescribed Treatment Course       | 34 (66.7)                 | 16 (18.4)                   | <0.0001|
| 30-day Readmission                          | 4 (7.8)                   | 11 (12.6)                   | 0.09|
| 90-day Readmission                          | 12 (23.5)                 | 21 (24.1)                   | 0.8 |
| Mortality, 30-day all-cause                 | 1 (2.0)                   | 1 (1.1)                     | 0.7 |
| Mortality, 1-year                           | 4 (7.8)                   | 1 (1.1)                     | 0.06|
| Length of Stay, days (median, IQI)          | 22.9 (9.8-42.7)           | 10.6 (6.0-17.4)             | <0.0001|
| Cost, Total Inpatient (USD; median IQI)     | 39220.90 (23300.71-82506.66) | 27592.39 (18509.45-48369.11) | 0.007|

Abbreviations: IQI = 25%-75% Interquartile range; HIV – Human Immunodeficiency Virus

*No longer statistically significant after adjusting for 5% false discovery rate using Benjamini-Hochberg method.*
Table 2. Comparison of DRA-OPAT Participants by pre- and post-implementation period

| Cohort                          | Pre-Implementation (2017) | Post-Implementation (2018) | p=  |
|---------------------------------|---------------------------|----------------------------|-----|
| Total N=                        | 31                        | 35                         |     |
| Age, years (median, IQI)        | 38 (35-45)                | 39 (29-49)                 | 0.94|
| Male, N (%)                     | 16 (51.6)                 | 19 (54.3)                  | 0.83|
| Race, Non-White                 | 26 (83.9)                 | 29 (82.9)                  | 0.92|
| Cocaine Use                     | 1 (3.2)                   | 2 (5.7)                    | 0.63|
| Opioid Use                      | 26 (83.9)                 | 28 (80.0)                  | 0.68|
| Polysubstance Use               | 26 (83.9)                 | 23 (65.7)                  | 0.06|
| Stimulant Use                   | 17 (54.8)                 | 23 (65.7)                  | 0.37|
| Medication for opioid use disorder | 21 (67.7) | 22 (62.9)                  | 0.68|
| Homeless                        | 13 (41.9)                 | 16 (45.7)                  | 0.94|
| HIV                             | 1 (3.2)                   | 0 (0)                      | 0.47|
| Hepatitis C                     | 16 (51.6)                 | 10 (28.6)                  | 0.03†|
| Charlson Comorbidity Index      | 20 (7.5-51)               | 23 (14.5)                  | 0.73|
| Cerebrovascular Disease         | 4 (12.9)                  | 3 (8.6)                    | 0.57|
| Congestive Heart Failure        | 9 (29.0)                  | 4 (11.4)                   | 0.07|
| Diabetes mellitus               | 3 (9.7)                   | 7 (20.0)                   | 0.31|
| Hepatic Disease                 | 14 (45.2)                 | 13 (37.1)                  | 0.37†|
| Chronic Pulmonary Disease       | 16 (51.6)                 | 11 (31.4)                  | 0.16|
| Kidney Disease                  | 5 (16.1)                  | 4 (11.4)                   | 0.72|
| Endocarditis                    | 16 (51.6)                 | 14 (40.0)                  | 0.34|
| Osteo-articular Infection       | 8 (25.8)                  | 15 (42.9)                  | 0.22|
| Skin / Soft Tissue Infection    | 14 (45.2)                 | 20 (57.1)                  | 0.33|
| Vertebro Abscess/Discitis/Osteomyelitis | 5 (16.1) | 10 (28.6)                  | 0.23|
| Staphylococcus aureus Bacteremia| 16 (51.6) | 17 (48.6)                  | 0.81|
| Bone or Joint Debridement†      | 3 (9.7)                   | 13 (37.1)                  | 0.02†|
| Cardiac Valve Replacement       | 2 (6.5)                   | 0 (0)                      | 0.13|
| Soft Tissue Debridement         | 8 (25.8)                  | 14 (40.0)                  | 0.32|
| Spinal Debridement              | 4 (12.9)                  | 3 (8.6)                    | 0.57|
| Infectious Disease Consult      | 28 (90.3)                 | 35 (100)                   | 0.1 |
| Completed Prescribed Treatment Course | 23 (74.2) | 16 (45.7)                  | 0.01|
| 30-day Readmission              | 2 (6.5)                   | 4 (11.4)                   | 0.68|
| 90-day Readmission              | 6 (19.4)                  | 9 (25.7)                   | 0.57|
| Mortality, 30-day all-cause     | 0 (0)                     | 0 (0)                      | --  |
| Mortality, 1-year               | 2 (6.5)                   | 0 (0)                      | 0.13|
| Length of Stay, days (median, IQI) | 35.1 (16-74.6) | 12.1 (8.9-17.9)            | <0.0001 |
| Cost, Total Inpatient ($USD, median [IQI]) | 68748.20 (34485.35-112712.08) | 33231.88 (24170.49-46670.35) | <0.0001 |

Abbreviations: IQI - 25%-75% Interquartile range; HIV – Human Immunodeficiency Virus

†No longer statistically significant after adjusting for 5% false discovery rate using Benjamini-Hochberg method.
Table 3. DRA-OPAT Participants by program completion

| N= | Completed DRA-OPAT | Did Not Complete Program |
|----|--------------------|-------------------------|
| Age, years (median, IQI) | 35 (28-53.3) | 40 (34-49) |
| Male, N (%) | 9 (56.3) | 10 (52.6) |
| Race, Non-White | 1 (6.3) | 5 (26.3) |
| Cocaine Use | 1 (6.3) | 1 (5.3) |
| Opioid Use | 15 (93.8) | 13 (68.4) |
| Polysubstance Use | 8 (50) | 14 (73.7) |
| Stimulant Use | 8 (50) | 15 (78.9) |
| Medication for opioid use disorder* | 14 (87.5) | 8 (42.1) |
| Homeless* | 12 (75) | 8 (42.1) |
| Insured | 1 (6.3) | 6 (31.6) |
| Charlson Comorbidity Index | 32 (12.5) | 20 (12.3) |
| HIV* | 0 (0) | 0 (0) |
| Hepatitis C | 4 (25) | 5 (26.3) |
| Cerebrovascular Disease | 1 (6.3) | 2 (10.5) |
| Congestive Heart Failure | 0 (0) | 4 (21.1) |
| Diabetes mellitus | 2 (12.5) | 5 (26.3) |
| Hepatic Disease | 5 (31.3) | 7 (36.8) |
| Chronic Pulmonary Disease | 6 (37.5) | 6 (31.6) |
| Kidney Disease | 2 (12.5) | 2 (10.5) |
| Endocarditis | 7 (43.8) | 7 (36.8) |
| Osteo-articular Infection | 6 (37.5) | 8 (42.1) |
| Skin / Soft Tissue Infection | 12 (75) | 8 (42.1) |
| Vertebral Abscess/Discitis/Osteomyelitis | 6 (37.5) | 4 (21.1) |
| Staphylococcus aureus Bacteremia | 8 (50) | 9 (47.4) |
| Bone or Joint Debridement | 7 (43.8) | 5 (26.3) |
| Cardiac Valve Replacement | 0 (0) | 0 (0) |
| Soft Tissue Debridement | 6 (37.5) | 7 (36.8) |
| Spinal Debridement | 2 (12.5) | 1 (5.3) |
| Hospital Length of Stay, days (median, IQI)* | 13.5 (10.6-18.5) | 9.1 (7.7-13.4) |
| Days at Program Facility* | 24 (19.5-38) | 4 (2-9) |
| 30-day Readmission | 2 (12.5) | 2 (10.5) |
| 90-day Readmission | 5 (31.3) | 4 (21.1) |
| Mortality, 30-day all-cause | 0 (0) | 0 (0) |
| Mortality, 1-year | 0 (0) | 0 (0) |
| Positive Toxicology Screen during Program | 0 (0) | 2 (10.5) |
| PICC Line Abuse | 0 (0) | 2 (10.5) |
| Adverse Event during Program Treatment | 3 (18.8) | 4 (21.1) |

Abbreviations: IQI – 25%-75% Interquartile Interval; HIV – Human Immunodeficiency Virus; PICC – Peripherally Inserted Central Venous Catheter

*Significant at p<0.05
Figure 1. Cohort Discovery and Pre- and Post-Implementation Patient Cohorts
