

A Proposal for Addiction and Infectious Diseases Specialist Collaboration to Improve Care for Patients With Opioid Use Disorder and Injection Drug Use Associated Infective Endocarditis

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Patients with injection drug use-associated infective endocarditis and opioid use disorder often receive treatment for the infection that fails to address its underlying cause. People who inject drugs (PWID) and develop serious infections also face disparities in antibiotic management, particularly with regards to use of outpatient parenteral antimicrobial therapy (OPAT). We highlight literature on OPAT in PWID challenging the notion that PWID cannot be managed with OPAT. Given that OPAT use amongst PWID and non-PWID yields similar outcomes, we argue that a bias against OPAT use in PWID is unwarranted and may reflect stigma rather than data. We further note the proven value of comprehensive OUD treatment on endocarditis treatment outcomes, which also addresses the potential safety concerns of OPAT in PWID, and propose a treatment model in which Addiction and Infectious Disease specialists collaborate to integrate opioid use disorder treatment into injection drug use-associated infective endocarditis care.

Key Words: infective endocarditis, injection drug use, opioid use disorder, outpatient parenteral antimicrobial therapy, PICO

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Injection drug use (IDU) is a risk factor for severe infections including infective endocarditis (IE) and hospitalizations for IDU-associated IE are rising. Unfortunately, patients with IDU-IE and OUD frequently receive care focused on OUD sequela (ie, endocarditis) while failing to address the underlying cause. In 1 study of patients with OUD and *Staphylococcus*

aureus bacteremia (43% with IDU-IE), 98% received an infectious diseases consultation, 100% received an echocardiogram, and 100% received an appropriate duration of antibiotic therapy; in contrast, 74% received treatment for their substance use disorder beyond recommendation of abstinence, 29% received a psychiatry consult, and only 2% discharged with a clear plan for ongoing outpatient addiction care.¹ Among a sample of patients hospitalized for IDU related infections, Jicha et al found that less than one-fifth of patients had any form of outpatient SUD treatment recommended by primary teams on discharge despite frequent recommendation of “cessation” of substance use.²

People who inject drugs (PWID) and develop serious injection-related infections (SIRIs) face disparities in antibiotic management. Standard treatment for IE consists of prolonged (2–6 week) courses of intravenous (IV) antibiotics via a long-term catheter, often completed at home in a practice termed outpatient parenteral antimicrobial therapy (OPAT). PWID have traditionally been excluded from this model of treatment due to concern for misuse of the IV catheter to inject drugs, precipitating venous thrombosis, catheter-associated bloodstream infection, or other complications.³ As an alternative approach, prolonged hospitalization for IV antibiotic therapy is limited by cost and patient nonadherence, particularly when the underlying substance use disorder is not addressed. Here, we highlight the literature supporting OPAT in PWID and propose a treatment workflow in which Infectious Disease and Addiction specialists collaborate to integrate OUD treatment into IDU-IE care.

WHAT ARE THE OUTCOMES OF OPAT IN PATIENTS WHO INJECT OPIOIDS?

Recent data challenge the notion that PWID cannot be treated with OPAT. Suzuki et al identified 10 studies (2 prospective, 8 retrospective) examining OPAT outcomes in PWID, most of which enrolled patients with active or recent (ie, within the past year) IDU.³ Specific substance use disorder interventions were offered infrequently in these studies, including drug counseling (n = 3), group treatment (n = 2), urine toxicology screening (n = 2), opioid therapy (n = 1), and a comprehensive harm reduction framework including sterile

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injection equipment, training, and rescue naloxone ($n = 1$). Despite this, rates of OPAT treatment completion ranged from 72% to 100%, comparable to or better than OPAT completion rates reported among non-PWID.⁴ Mortality during OPAT was 0% in 7 studies and 2%–10% in the remaining 3; of note, in the study reporting a 10% mortality rate, mortality was no better in a comparator population of non-PWID receiving OPAT.³ The 3 studies reporting documented catheter manipulation noted rates of 0%–2% and no difference in line infection between PWID and non-PWID receiving OPAT. Data of OPAT in PWID receiving concurrent addiction treatment is even more encouraging; Price et al, reporting a cohort of 68 such patients, noted 100% antibiotic completion without a single episode of overdose, death, or catheter-related complication.⁵

Finally, while other evidence suggests that OPAT for PWID may be more labor-intensive compared to non-PWID, patient-centered outcomes remain similar. Comparing 159 PWID to 6493 non-PWID treated with OPAT for serious infections, Dobson et al reported PWID had higher incidences of after-hours calls for telephone consultation to troubleshoot catheter complications and accidental dislodgements, but no difference versus non-PWID in all-cause catheter removal for thromboses, bloodstream infections, or other complications. In addition, 98% of PWID completed their treatment, and only a single patient was readmitted to the hospital.⁶

We conclude that robust data suggests OPAT, the current standard of care for serious infections like IE in non-PWID, achieves similar outcomes with similarly low rates of adverse events in PWID. Thus, a preference for alternative antimicrobial approaches in PWID versus non-PWID is not justified. Moreover, rates of discharge against medical advice among patients with OUD admitted for IE have been reported as high as 34%–48%; hence, shortened hospitalizations facilitated by OPAT may improve overall quality of care in this population even where rates of OPAT noncompletion, catheter misuse, and other complications are high.⁷

WHAT CAN BE DONE TO IMPROVE OUTCOMES OF OPAT IN PATIENTS WHO INJECT OPIOIDS?

Efforts to optimize OPAT outcomes in PWID largely consist optimizing patient selection for OPAT and comprehensively managing the underlying OUD. A review of 679 patients treated for IDU-IE found that initiation of pharmacotherapy for OUD within 30 days of discharge was associated with substantial reduction in all-cause mortality at 1 year after discharge (adjusted hazard ratio 0.30; 95% confidence interval 0.1–0.89).⁸ Inpatient pharmacotherapy for OUD in patients with SIRS has also been associated with significant reductions in against medical advice discharge.⁷ Fanucchi et al report a model of integrated OUD and IDU-IE care with opioid agonist treatment and OPAT achieved infection cure and substance use outcomes similar to or better than usual care while also achieving a >3 week mean reduction in length of stay.⁹ Importantly, Suzuki et al showed that the majority of inpatients with OUD and IE are receptive to medication for opioid use disorder (MOUD) when offered by addiction specialists.¹⁰

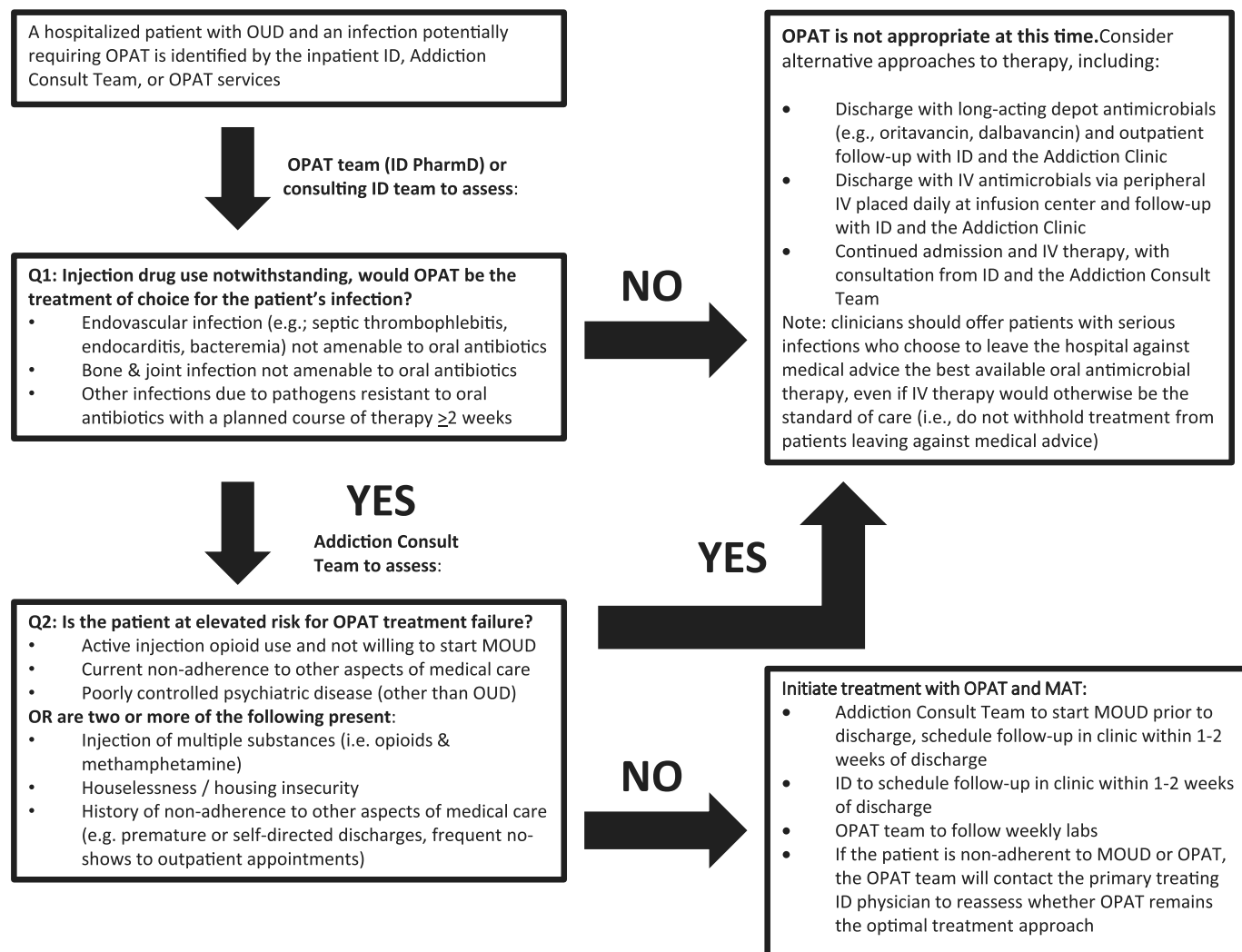
Evidence-based identification of patients at highest risk of complications and treatment noncompletion may improve OPAT outcomes. PWID with housing instability are more likely to have evidence of line tampering, develop secondary bloodstream infection, and have a 30-day readmission related to OPAT versus their non-PWID and housed PWID peers.¹¹ Eaton et al validated a 9-point risk assessment tool for OPAT treatment failure in PWID, which included active cravings, unstable home environment, co-occurring psychiatric diagnosis, history of drug overdose or multiple relapses, polysubstance use, family history of addiction, history of trauma, and limited willingness to change.¹² The authors offered OPAT to PWID defined as “low-risk” (≤ 3 points on their assessment tool), reporting significant reductions in mean LOS and cost savings with no increased rate of readmission with this intervention.

Improving outcomes in patients with IDU-IE will require multidisciplinary efforts to actively treat OUD, mitigate potential clinician bias with evidence-based screening tools that assess likelihood of OPAT success, and engage social work and public health services to address social determinants of health. Early engagement of patients in addiction treatment via inpatient addiction consultation services is likely a key strategy to reducing recurrent hospitalizations for OUD-associated endocarditis.¹³

FUTURE DIRECTIONS AND MODELS OF CARE

We propose a collaborative care model incorporating physician and pharmacist specialists in Addiction and Infectious Diseases into a comprehensive approach to MOUD and OPAT in patients with IDU-IE and other SIRIs requiring prolonged IV antibiotic therapy. This model should emphasize short-term follow-up and planning for outpatient continuation of MOUD to improve adherence to both MOUD and OPAT. We have adopted such a workflow at the University of Nebraska Medical Center, which could be adapted to fit other institutions based on local patient populations and their needs (Fig. 1).

In implementing this workflow, we encountered obstacles that clinicians at other institutions should anticipate. First, many of our patients with OUD have concurrent injection methamphetamine use, a disorder for which both treatment options and data on OPAT success and safety are far more limited. A contingency management approach, in which patients receive financial or other incentives to abstain from injection methamphetamine use, has been described but not reported in the context of infection; we believe applying this approach for patients who inject methamphetamine and are receiving OPAT merits further study.¹⁴ Second, resistance to a collaborative model of care from hospital leadership, home infusion services, or both may arise out of concern for medicolegal risk if a catheter is misused. To address these concerns, we recommend adopting a formal institutional protocol congruent with scientific evidence (such as those cited here), and endorsed by key stakeholders including Infectious Diseases, Addiction Medicine and/or Addiction Psychiatry, and OPAT team leaders, and the institutional legal team.



Legend:

OUD= Opioid Use Disorder; IV= intravenous; ID = Infectious Diseases; OPAT= Outpatient Parenteral Antimicrobial Therapy;

MOUD = Medication for Opioid Use Disorder

FIGURE 1. The University of Nebraska Medical Center Collaborative Model.

Such a workflow is likely to require continuous reevaluation and revision as standards of care for OUD and IE treatment (in all patients, not just PWID) continue to evolve. For instance, new data support early transition to oral antibiotics for IE, which may obviate the need for OPAT in at least some of these cases.¹⁵ Novel long-acting IV antibiotics (eg, dalbavancin) may allow effective SIRI treatment without a long-term catheter, and present an opportunity for psychiatrists to share their experiences with infectious disease colleagues, as the former have managed patients with depot antipsychotics in the ambulatory and home settings for many years. Finally, formal multidisciplinary endocarditis teams including cardiothoracic, infectious disease, and addiction specialists, and patient-centered treatment planning conferences, may improve IE outcomes.

CONCLUSIONS

OUD and IDU-IE are concurrent public health crises that require effective, multidisciplinary care focused on treating both diagnoses. Given that OPAT use amongst PWID and non-PWID yields similar outcomes and is likely superior to attempting prolonged hospitalization for PWID with IE, general preference against OPAT in PWID is unwarranted. Clinicians should address bias against PWID by embracing evidence-based protocols for OPAT and comprehensive OUD treatment in this setting- and ultimately, by advocating for public policy facilitating harm reduction to limit the complications of IDU.

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