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EDITORIAL COMMENTARY

Co-located Opioid Use Disorder and Hepatitis C Virus Treatment Is Not Only Right, But It Is Also the Smart Thing To Do as It Improves Outcomes!

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(See the Major Article by Rosenthal et al on pages 1715–22.)

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The opioid epidemic in the United States [1, 2] has been associated with a rise in new infectious diseases among persons who use drugs (PWUD), including invasive bacterial and fungal infections [3–6], new human immunodeficiency virus (HIV) outbreaks [7–9], as well as numerous hepatitis C virus (HCV) outbreaks [10, 11] that are occurring in particular among younger populations 18–24 years old. Medication treatments for opioid use disorder (MOUD) (eg, buprenorphine, methadone, and extended-release naltrexone [XR-NTX]) are efficacious in reducing opioid use, overdose, and HCV and HIV transmission. Recent advances in HCV treatment allow us to safely and effectively cure HCV even among PWUD and among those who are on MOUD [12–15]. However, despite this, few studies have evaluated the effectiveness of integrated HCV and opioid use disorder (OUD) treatment on both drug and HCV outcomes in a real-world setting. In this issue of *Clinical Infectious Diseases* Rosenthal and colleagues [16] report on the Hepatitis C Treatment to Prevent HIV, Initiate Opioid Substitution Therapy, and Reduce Risky Behavior (ANCHOR) study, a prospective, open-label, observational trial in which HCV therapy and MOUD care were integrated.

One hundred participants with OUD and HCV infection were followed for 24 weeks. All were initiated on direct-acting antiviral (DAA) treatment with sofosbuvir/velpatasvir and had 12-week sustained viral response (SVR) outcome measurements. In addition. all participants were offered integrated buprenorphine treatment for their OUD at the same time as the HCV treatment and could opt to start at any time during the 24-week study period.

It is notable that 93% of the participants in this study were African American (AA), 51% were unstably housed, and 33% had comorbid HIV infection. The fact that there was a high proportion of AA persons is important as few HCV treatment trials have included significant minority populations, yet AA and minority populations are less likely to be referred for HCV treatment or offered DAAs and are at higher risk of death due to lack of access to care as compared with Caucasian populations [17, 18].

Importantly as well, the majority of participants (82%; n = 82) achieved 12-week SVR, which is similar to other trials of PWUD who initiated DAAs for HCV such as in the Prevent Resistance Eliminate Virus And Improve Live (PREVAIL) trial [19]. Of the 18% (n = 18) in this study who did not achieve 12-week SVR, 11 of them had viral rebound. There was no association of achieving SVR with receipt of buprenorphine at baseline, concurrent illicit drug use, or poor DAA adherence, but completing 2 or more bottles of DAA treatment and retention on buprenorphine at week 24 was associated with achieving SVR. This is an important point: DAA adherence, MOUD receipt, and retention on MOUD were associated with achieving SVR and hence, a cure of HCV. These findings are consistent with those of other studies that have demonstrated similar findings among persons with HIV (PWH) and concurrent OUD who were started on MOUD including buprenorphine and XR-NTX [20–23]. A prospective, observational, open-label nonrandomized trial of buprenorphine administered along with antiretroviral therapy (ART) in PWH with OUD identified that retention on buprenorphine at 24 weeks predicted HIV viral suppression (VS) at less than 50 copies/mL [20]. Further, 2 double-blinded, placebo-controlled trials of XR-NTX among PWH with high rates of comorbid HCV infection demonstrated that those who received XR-NTX for (1) OUD [21] or (2) alcohol-use disorder [22] were

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statistically significantly more likely to achieve and maintain maximal VS at 24 weeks after initiation as compared with those who received placebo. Thus, integrating infectious disease treatment (ART for HIV and DAAs for HCV) with MOUD for OUD treatment can improve both outcomes. Given the World Health Organization's goal is to end HCV by 2030 [24] as is the US goal to end HIV by 2030 [25], there must be a concerted effort to ramp up integrated infectious disease and OUD treatment. However, it is rare that programs integrate OUD treatment and infectious diseases prevention and care. The National Academies of Sciences, Engineering, and Medicine has recently issued a report that provides recommendations for this integration to take place [26].

Another important finding from the study by Rosenthal et al is that ongoing drug use was not associated with impairing the likelihood of achieving SVR and hence HCV cure. Thus, yet again, this study drives home the point that continued drug use should not be a reason to withhold HCV treatment. It is clear, however, that offering MOUD for those with concurrent OUD can help achieve SVR in addition to reducing morbidity and mortality from ongoing opioid use if retained on a form of MOUD. Clinicians should therefore continually be assessing patients for ongoing substance use and diagnosis of OUD to initiate effective treatment. In this study, despite 100% having OUD, only 33% were on MOUD at the initial screening stage of this study, thus identifying a huge gap in initiation of treatment for OUD. However, 79% of the participants initiated buprenorphine while undergoing DAA treatment and there was a doubling of participants (68%) who were on treatment at the end of the 24-week period as compared with 33% at baseline. This highlights the important point of continually assessing patients' needs and interest in initiating MOUD, which may be at the beginning of HCV or other infectious disease treatment, or in the middle or the end of treatment.

Drug-use behavior, not surprisingly in this study, continued as has been shown in other studies of HCV treatment as well as in those receiving HIV treatment among PWUD while on effective forms of MOUD. The majority of participants in this study (89%) used opioids based on urine drug screens (UDSs), and 61% used cocaine with over three-quarters of the participants endorsing IDU behavior. It is well established that craving for a drug in a person with a substance-use disorder (SUD) can occur despite effective treatment even in those with OUD receiving MOUD. What is more important about this study is that ongoing drug use did not interfere with HCV treatment achieving SVR/cure, similar to other studies, but also that participants were retained on buprenorphine treatment despite ongoing drug use. The investigators also demonstrated that there was a decline in opioid-positive UDSs and a reduction in high-risk behaviors in those persons who started and were retained on MOUD treatment while receiving HCV treatment. Other studies have clearly demonstrated that MOUD reduces risk behaviors [27, 28]. Thus, not only can MOUD improve HCV but it can also reduce high-risk behaviors that could lead to reinfection with HCV, which has been shown with the PREVAIL Extension study [29, 30].

This study also identified that 13% (n = 13) experienced at least 1 overdose during the 24-week study period, of which 2 were fatal. Importantly, those who were not on buprenorphine or other form of MOUD had a statistically significantly higher rate of overdose (26%) compared with those who were on buprenorphine. Further UDSs identified that polysubstance use including fentanyl and cocaine is common, and co-located SUD and HCV treatment provides another opportunity to offer other harm-reduction services in addition to MOUD, such as syringe-exchange services, opioid overdose education, naloxone distribution, fentanyl testing strips, as well as other forms of behavioral treatment for other SUDs that do not yet have effective medication treatments like stimulant-use disorders.

One limitation of this study was that the dose of buprenorphine was not provided, and it is possible that suboptimal dosing led to ongoing drug use and should be considered in future studies as well as considering evaluation of once-monthly injectable forms of MOUD such as long-acting subcutaneous injectable monthly buprenorphine (Sublocade, Indivior Inc.) or once monthly intramuscular injection of XR-NTX (Vivitrol, Alkermes Inc.), as well as the buprenorphine implant that lasts 6 months (Probuphine, Titan Pharmaceuticals). All of these long-acting forms of MOUD theoretically could overcome potential barriers like adherence to oral forms of MOUD and suboptimal dosing of methadone and buprenorphine when treating OUD and infectious diseases like HCV, HIV, and bacterial infections among PWUD.

Overall, the ANCHOR study [16] identifies, importantly, that cotreating infectious diseases and SUDs can lead to reduced morbidity and mortality from 2 diseases. Infectious disease clinicians are highly prepared for providing such integrated care as they have demonstrated in caring for PWH in Ryan White–funded clinics that provide wraparound services including SUD treatment. In order to end the opioid and associated infectious disease epidemics in this country and globally, screening and diagnosis of OUD and other SUDs along with initiation of SUD-effective treatment must be linked with screening, diagnosis, and treatment of HCV to end the HCV epidemic globally [26, 31–33].

Notes

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