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Prescribe to Save Lives: Improving buprenorphine prescribing among HIV clinicians

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Abstract

Background: HIV clinicians are uniquely positioned to treat their patients with opioid use disorder (OUD) using buprenorphine to prevent overdose death. The Prescribe to Save Lives (PtSL) study aimed to increase HIV clinicians' buprenorphine prescribing via an overdose prevention intervention.

Methods: The quasi-experimental stepped wedge study enrolled 22 Ryan White funded HIV clinics and delivered a peer-to-peer training to clinicians with follow-up academic detailing that included overdose prevention education and introduced buprenorphine prescribing. Site-

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aggregated electronic medical record (EMR) data measured with the change in X-waivered clinicians and patients prescribed buprenorphine. Clinicians completed surveys pre-intervention and at 6- and 12-months post-intervention that assessed buprenorphine training, prescribing, and attitudes. Analyses applied Generalized Estimating Equation models, adjusting for time and clustering of repeated measures among individuals and sites.

Results: Nineteen sites provided EMR prescribing data, and 122 clinicians returned surveys. Of the total patients with HIV across all sites, EMR data showed 0.38% were prescribed buprenorphine pre-intervention and 0.52% were prescribed buprenorphine post-intervention. The intervention increased completion of a buprenorphine training course (AOR 2.54, 95% CI 1.38–4.68, p=0.003) and obtaining an X-waiver (AOR 2.11, 95% CI 1.12–3.95, p=0.02). There were non-significant increases at the clinic level, as well.

Conclusion: Although the PtSL intervention resulted in increases in buprenorphine training and prescriber certification, there was no meaningful increases in buprenorphine prescribing. Engaging and teaching HIV clinicians about overdose and naloxone rescue may facilitate training in buprenorphine prescribing, but will not result in more treatment with buprenorphine without additional interventions.

Keywords

HIV; opioid use disorder; buprenorphine; intervention study; clinician education; overdose prevention

INTRODUCTION:

HIV infection and opioid use disorder (OUD) together are syndemic – and individuals are at high risk for fatal overdose.[1] Opioid overdose is more common and more deadly among people living with HIV (PLWH) than those without HIV.[2] Using the National HIV Surveillance System, from 2011 to 2015, there was a 42.7% increase in the rates of opioid overdose in PLWH[3]. Among people who use drugs, HIV seropositivity has been associated with a 74% increased risk of overdose mortality.[2] PLWH are also more likely than people without HIV to have chronic pain and be treated with chronic opioid therapy,[4] which may contribute to their heightened overdose risk. Alongside the COVID-19 pandemic, the overdose epidemic has rampantly worsened, and it is certain that PLWH have not been spared.

Buprenorphine can be prescribed in primary care, is dispensed at community pharmacies, and has robust evidence to treat OUD and reduce overdose and all-cause mortality.[4–9] The strong evidence that buprenorphine saves lives has led to recent national increases in buprenorphine treatment fueled primarily by non-specialists[10], yet substantial gaps in prescribing clinician capacity still exist[11]. To prescribe buprenorphine for OUD, physicians were required to be board certified in addiction psychiatry or addiction medicine or take 8-hours of training certified by Substance Abuse and Mental Health Services Administration (SAMHSA), and nurse practitioners and physician assistants were required to take 24 hours of training certified by SAMHSA. Then, they can register with the Drug Enforcement Administration (DEA) under the federal Drug Addiction Treatment Act of 2000 for an

X-waiver that allows them to prescribe. The training requirement was removed for clinicians treating up to 30 patients in 2021, though registering with the DEA for an X-number is still required. As of 2018, 45% of U.S. counties had no X-waivered clinicians[12,13] and, according to the SAMHSA (as of March 2021), merely 9% of all professionally active U.S. physicians had a waiver to prescribe buprenorphine.[14,15] Practice guidelines have changed as of April 2021 for certain clinicians who no longer have to attend a training in order to obtain an X-waiver and can prescribe buprenorphine to a limited number of patients[16].

HIV care clinicians are uniquely positioned to treat OUD with buprenorphine and prevent overdose death. National organizations including the National Institutes of Health, Infectious Disease Society of America, HIV Medicine Association, and the National Academies of Sciences, Engineering, and Medicine have advocated for a concerted, interdisciplinary Addiction Medicine and Infectious Diseases treatment approach.[17–19] Yet, several barriers to prescribing buprenorphine exist among HIV clinicians, including concern for lack of access to addiction experts, less confidence in addressing drug problems, staff training, access to counseling, visit time, buprenorphine availability in community pharmacies.[20–25] A variety of models have been attempted to integrate buprenorphine treatment into HIV care settings[26], and when surveyed, Infectious Disease physicians agree that they should be actively managing SUDs; however, they receive little training to do so.[17] When clinicians start PLWH on buprenorphine for their OUD, patients have increased engagement in addiction treatment,[27] increased probability of viral suppression,[28] and clinical HIV outcomes comparable to those without OUD.[29–31] Buprenorphine has few drug-drug interactions with antiretroviral therapy, low overdose risk, and no requirement for daily observed dosing, making it cost-effective and feasible for HIV clinicians to prescribe in their clinics.[32] Despite the national calls of action to integrate systems of care and HIV clinician's acceptability to prescribe buprenorphine, a study across five U.S. states showed that PLWH in general, had a lower probability of being on medications for OUD like buprenorphine than those without HIV.[33]

Previous studies have shown that HIV clinicians were resistant when directly approached to adopt buprenorphine to treat opioid dependence[34]. The Prescribe to Save Lives Study (PtSL) designed, implemented, and evaluated an on-site training intervention of overdose education packaged with academic detailing aimed to engage HIV clinicians to prescribe naloxone for overdose prevention and indirectly encourage them consider prescribing buprenorphine to treat OUD. PtSL used a stepped-wedge design in 22 outpatient Ryan White-funded federally qualified health center HIV clinics. The aim of the current study was to determine the effectiveness of the PtSL intervention among HIV clinicians in prescribing buprenorphine to PLWH with OUD. The hypothesis was that HIV clinicians receiving the PtSL intervention would be more likely to prescribe buprenorphine for OUD.

METHODS:

Study Design:

Determining the effectiveness of the PtSL intervention to get HIV clinicians to prescribe buprenorphine was a pre-specified aim in the stepped-wedge trial. PtSL was initially designed as a 3-wave, cluster-randomized, one-way cross-over design trial that required

modification to meet enrollment and timeline targets, so that the waves were not randomized but instead were selected in order of recruitment. Inclusion criteria were applied to the clinic sites. For clinicians to be included, they needed to be a prescribing clinician (MD, Nurse Practitioner, or Physician Assistant) at a study site that agreed to participate. Sites were encouraged to invite all prescribers to participate.

Site eligibility criteria included: (1) receive Ryan White HIV Funding; (2) treat adults with HIV; (3) have 3 or more prescribing clinicians willing to participate; and (4) have an electronic medical record (EMR) with an electronic medication list, (5) are in states with the high rates of fatal opioid overdoses based on 2008 based on CDC surveillance data. Sites from states with fewer than 500 PLWH were excluded from participating.

Enrolled sites received mailed literature and promotional materials providing the rationale for fatal overdose prevention in the HIV population 1 week prior to intervention which was followed by an on-site peer-to-peer 1.5-hour training by a physician expert that provided Continuing Medical Education credits and focus on saving lives through overdose education and naloxone prescription. The training was adapted from didactics that co-authors had previously developed to train health care providers and others in overdose education and naloxone prescription[35] and included written materials, brief lecture, discussion, demonstrations, and brief role-play to provide HIV clinicians with the epidemiological rationale and empirical evidence for overdose education, train them in how to discuss overdose with their HIV patients and prescribe naloxone, as well as introduction that office-based buprenorphine treatment can treat the primary disease of opioid addiction. The intervention did not include a buprenorphine specific training. This study was designed using a conceptual model of implementation research to specifically test a well-established, and proven implementation strategy – academic detailing. In-person or telephone academic detailing occurred 1-, 3-, 5-months post-training to reinforce the value of naloxone prescription and use motivational techniques to increase clinician readiness to prescribe buprenorphine. The PtSL study took an indirect approach based in the ethos of saving lives through naloxone rescue to inspire providers to engage further in care of patients with OUD by treating them with buprenorphine. By first training HIV clinicians to prescribe naloxone to patients at risk for overdose and educate them to reduce their overdose risk and then providing academic detailing strategy to overcome HIV clinicians' resistance[34] to accept addiction treatment as within their professional scope, the project sought to increase both naloxone and buprenorphine prescribing.

Study Participants:

Clinical providers (N=122) from 22 Ryan White funded HIV primary care clinics who enrolled in PtSL from August 2017 to December 2019 were included in the analysis. Enrolled clinicians completed a baseline assessment and follow-up assessments at 6- and 12-months post-intervention. The study was approved by the Baystate Medical Center and The Miriam Hospital Institutional Review Boards and registered at ClinicalTrials.gov (NCT03175640).

Study Measures

These analyses used (1) aggregate electronic medical record (EMR) data provided by sites across five time periods from before study start to study end and (2) self-reported responses to surveys completed by clinicians at baseline and at 6- and 12- month follow-up after the initial training at each site. Time periods for data collection are described in Supplement 1.

Characteristics of clinicians and their practices, including clinician demographics (gender, race, ethnicity, age), clinician type, if they cared for at risk patients (defined as > 10% of patients treated with chronic or acute opioids, have OUD or are using injection drugs) as well as how often they assessed for illicit opioid use or injection drug use most or all of the time, years providing care for patients with HIV, percent of clinical time caring for patients with HIV, number of patients with HIV in direct care, and hours per week of patient care were collected through the survey.

The primary outcome was clinic-level prescribing of buprenorphine (defined as receiving 1 buprenorphine prescription as confirmed via EMR) including the proportion of patients with HIV being prescribed buprenorphine per clinic and the proportion of clinics having at least one clinician prescribing buprenorphine. We determined the pre-post intervention buprenorphine prescribing rate from each site's EMR using de-identified aggregate data which included total number of patients with HIV served by the clinic, number of patients with HIV prescribed buprenorphine per clinic, and number of clinicians who prescribed buprenorphine per clinic.

Secondary outcomes focused on clinician self-reported buprenorphine prescribing behaviors and included the proportion of clinicians who prescribed buprenorphine, attended a buprenorphine waiver training, and obtained an X-waiver from the DEA. We assessed self-reported clinician buprenorphine prescribing via baseline and follow-up surveys where clinicians were asked if they had prescribed any of the following three types of buprenorphine products to their patients for treatment of OUD: buprenorphine with or without naloxone (Suboxone®/Subutex®), implantable buprenorphine (Probuphine®), or long-acting injectable buprenorphine (Sublocade®). We assessed clinician self-reported attending buprenorphine waiver training and obtaining an X-waiver via baseline and follow-up surveys.

Additionally, we assessed four clinician attitudes towards buprenorphine prescribing including interest, confidence, readiness, and commitment to prescribe buprenorphine by using 0–100 visual analog scale change readiness rulers (0: Not at all – 100: Extremely) which have been previously used in motivational interviewing[36] studies and have performed as well or better than more elaborate readiness to change questionnaires in predicting behavioral intentions [37].

Statistical analysis

Participating clinician demographics and clinical practice measures, as well as site buprenorphine prescribing numbers, were reported using descriptive statistics including means and standard deviations or frequencies and percentages. To determine intervention effects for both EMR and survey data outcomes marginal effects models were fit.

Generalized estimating equation (GEE) population-averaged models included variables for intervention (pre/post) and calendar time period. Each model also specified correlated outcomes due to clustering (repeated measures on individuals/sites) and used an appropriate link function for the given outcome. Five calendar time periods, the first coinciding with pre- wave 1 baseline survey administration and the last coinciding with the 3rd wave's final follow-up, were coded as a series of categorical indicators to allow for non-linear trends.

RESULTS:

We surveyed a total of 122 clinicians from 22 different clinics across 18 states in the U.S (Supplement 1). The number of HIV clinicians per site ranged from 2 to 27, with a mean of approximately 5 HIV clinicians per site during the study period. Overall, 119 clinicians completed a baseline survey, 111 and 94 completed a 6- month and 12-month survey, respectively. The 6-month retention was 91%, and 90 (76%) clinicians completed all 3 surveys.

HIV clinicians were split evenly between physicians (MD) and advanced practitioners (Nurse Practitioners, Physician Assistants). A majority was female and white, with a mean age of 43 years. On average, clinicians had been working with patients with HIV for almost a decade and had 155 patients with HIV under their direct care, 68% cared for at-risk patients with HIV, and 84% assessed for illicit opioid use or injection drug use (Table 1).

We acquired EMR data from 19 of 22 sites. Three sites from wave 3 were unable to provide any EMR data and, in addition, one of the 19 compliant sites was not able to provide useable data only for the number of clinicians prescribing buprenorphine.

HIV Clinician Buprenorphine prescribing

EMR data showed the total number of patients with HIV across all sites seen during pre-intervention time periods was 44,607, and the number seen during post-intervention time periods was 66,756. Of these patients, 171 (0.38%) were prescribed buprenorphine pre-intervention, and 344 (0.52%) were prescribed buprenorphine post-intervention. The number of sites that had at least one patient with HIV prescribed/clinician prescribing buprenorphine was 9 (47%) before intervention and 12 (63%) after intervention. The mean number of clinicians prescribing buprenorphine per site was 1.89 pre-intervention and 2.89 post-intervention. The post intervention absolute number of patients with HIV prescribed buprenorphine (per 100 HIV patients) and number of clinicians prescribing buprenorphine per clinic over the course of the study showed small, increases for some clinics (Supplement 2).

GEE models using EMR data indicated small effect sizes for buprenorphine prescribing post-intervention compared to pre-intervention, which were in the expected direction but were not statistically significant. In terms of our primary outcome, the post-intervention adjusted odds ratio (AOR) of a patient with HIV being prescribed buprenorphine was 1.47 (95% CI 0.50–4.28, p = 0.49). The post-intervention AOR for a site having at least one clinician prescribing buprenorphine was 3.09 (95% CI 0.54 – 18.00, p = 0.21).

In terms of the secondary outcomes, survey data showed that 21% of clinicians self-reported prescribing buprenorphine at the pre-intervention, and 33% self-reported prescribing buprenorphine at the 12-month post-intervention follow up. The adjusted odds of self-reported buprenorphine prescribing by clinicians post- vs pre-intervention, was 1.63 (95% CI 0.78–3.41, p = 0.20) (Table 2). We found increases in both the number of clinicians completing a buprenorphine training course and obtaining an X-waiver post-intervention. The percentage of study enrolled clinicians who completed a buprenorphine training course increased from 34% to 55% (model AOR 2.54, 95% CI 1.38–4.68, p<0.01), and the percentage obtaining an X-waiver rose from 26% to 35% (AOR 2.11, 95% CI 1.12–3.95, p=0.02).

HIV Provider attitudes towards prescribing buprenorphine

Comparing post- vs pre-intervention clinician prescribing interest, confidence, readiness, and commitment on a 0 – 100 scale measure, the largest increases were seen in confidence in prescribing buprenorphine, with a mean increase of 12.27 (95% CI 0.69–23.84, p=0.04) points post- vs pre-intervention and buprenorphine prescribing readiness with a mean increase of 10.89 (95% CI −0.31–22.09, p=0.06) (Table 3). There were no changes in self-reported commitment to prescribe buprenorphine.

DISCUSSION:

This study of implementing an on-site, peer-to-peer training and academic detailing intervention to promote prescribed medications that reduce overdose death did not have clinically significant improvements in buprenorphine prescribing measured both at the clinic-level through EMR and by clinician self-report. We found that among the study clinics, buprenorphine prescribing was very low and did not substantively change with an intervention focused on preventing the most devastating consequence of OUD, a fatal opioid overdose. Prior efforts to increase clinician buprenorphine prescribing have had limited applicability in that they had small sample sizes,[38] had varying implementation protocols[39], lacked a comparison group,[39,40] and, though feasible[40], had limited enthusiasm from HIV clinicians to adopt. [34] Despite disappointingly low rates of buprenorphine prescribing post-intervention, our findings are important and may inform future interventions aimed to bolster prescribing of medications for OUD by HIV clinicians.

The dearth and inaccessibility of primary and continuing clinician education in the management of substance use disorders has consistently been identified as a significant barrier to prescribing buprenorphine in the literature.[22,41] HIV clinicians, particularly those in practice for many years, must seek continuing medical education to learn new concepts on their own time. By bringing easy-to-access education directly to HIV clinicians within their clinical setting, our intervention aimed to eliminate one logistical barrier[42] but was not as comprehensive as a formal buprenorphine training course. Nonetheless, this intervention, more than doubled the HIV clinicians' odds of taking a buprenorphine training course and obtaining an X-waiver. Our finding suggests that using a training focused on overdose prevention was inadequate to change prescribing behavior yet may be a "foot in the door" strategy to encourage clinicians to contextualize the need to engage with their patients

with HIV and OUD and seek additional skills to adopt buprenorphine prescribing in their practice.

Prior literature has suggested that HIV clinicians have concerns about prescribing buprenorphine but after attending a formal buprenorphine training, most felt prepared to prescribe, planned to obtain an X-waiver[43], had increased confidence in addressing their patients' drug problems,[20] and recognize clinical appropriateness of buprenorphine prescribing.[21] At the time the study was conducted, clinicians needed to attend an 8 to 24 hour training in order to apply for the X-waiver.[42] Partly due to this regulatory barrier, nationally over 90% of clinicians have not attended a training.[44] Previous incentive strategies to motivate clinician attendance to buprenorphine trainings have included integration within graduate medical education which led to 27% trainees obtaining X-waiver [45] or providing a $750 financial compensation for training time which led to 89% completion of X-waiver training but low, highly-variable rates of prescribing buprenorphine.[46] Even though practice guidelines have removed the mandatory to attend a buprenorphine training prior to getting an X-waiver, our findings suggest that our isolated intervention may be an additional strategy to encourage HIV clinicians to obtain their X-waiver and prescribe buprenorphine. When assessing clinician attitudes towards buprenorphine prescribing, at baseline, HIV clinicians had only favorable interest and commitment in prescribing buprenorphine but post intervention, clinicians had overall higher self-confidence and greatest increase in self-confidence to prescribe buprenorphine; self-confidence alone, without greater motivation, logistical support, and resources, had insufficient impact on buprenorphine prescribing. Similarly, outside of trials, many waivered clinicians either prescribe to a minority of patients or not at all,[47,48] and lack of specialist support is a commonly cited barrier.[48] Future interventions should consider using a multipronged approach that supports clinicians to prescribe buprenorphine, especially those who care for higher risk patients. Previously studied support models that could be leveraged in this approach are the federally funded Providers Clinical Support System initiatives,[49,50] hub-and-spokes opioid treatment network model,[51] nurse care manager model of Office-Based Addiction Treatment,[52] pharmacist-provider collaborative care models for buprenorphine[53,54], and learning collaboratives like Project ECHOs' Integrated Addictions and Psychiatry TeleECHO Clinic.[55]

It is also important to explore alternative explanations for the disappointingly low overall amount of buprenorphine prescribed by HIV clinicians. It remains unknown if HIV clinicians can accurately screen for OUD[56] and there is also great variability on how comprehensive their assessments are and how much discomfort they experience when discussing topics about substance use[57]. Perhaps this is due to the historical siloing of addiction medicine away from mainstream medicine[18]. Furthermore, HIV clinicians rank addressing substance use lower than addressing medication adherence and HIV symptoms and treatment[58], and often rely on referrals to treatment at outside agencies[57] so it may be that prescribing buprenorphine is seen as less within their scope of clinical work. Patients with HIV often experience multiple layers of stigma[59] and this anticipated stigma of discussing substance use with their HIV provider possibly could influence if they disclose their use and or seek external addiction care.

These findings have important limitations. First, the planned upfront recruitment and randomization of Ryan White clinics proved infeasible, which constrained the ability to make causal inferences and missing EMR data from three clinics may have impacted the results. Second, we were unable to collect data on the total number of HIV clinicians at each clinic or whether the HIV clinicians who participated in the study were different than those who did not participate. Third, our study did not directly measure the prevalence of OUD or opioid analgesic prescribing at each site or within the state so we cannot account for any secular trends about these two over the study period. Fourth, based on study methods, we were unable to exclude clinicians who previously were X-waivered or prescribed buprenorphine and patients with HIV who may have been prescribed buprenorphine at external sites, which may have impacted our results for buprenorphine prescribed. Fifth, the study was based in federally funded Ryan White clinics so it may not be generalizable to other primary care offices. Finally, the clinicians' self-reports were subject to social desirability effects and secular prescribing trends which we attempted to control by adjusting our analysis for calendar time.

Despite these limitations, the study used a rigorous quasi-experimental design, included clinics from 18 different states, and had relatively complete follow-up clinic and clinician data. Perhaps an intervention such as PtSL which is focused on overdose prevention can be a first step to improving HIV clinicians' confidence to treat OUD and priming them to seek additional training in office-based buprenorphine care provision. While a limited educational intervention like PtSL may be sufficient to motivate clinicians to acknowledge the need for additional buprenorphine training, seek obtaining X-waiver, greater effects might be seen in future studies with more intensive, repeated, comprehensive educational interventions and/or different incentives.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1:

Characteristics of clinicians at 22 Ryan White-funded HIV clinics, August 2017 to December 2019 (n= 119)

Demographics	
Female, N (%)	86 (72.3)
Hispanic, N (%)	12 (10.1)
Race, * N (%)	
White	74 (62.2)
Black	22 (18.4)
Other	22 (18.4)
Age mean (years)	43.3 (9.7)
Clinician type, N (%)	
Physician	57 (47.9)
Nurse Practitioner	49 (41.2)
Physician Assistant	9 (7.6)
Missing	4 (3.4)
Clinician characteristics, N (%)	
Care for at-risk patients with HIV **	68 (60.7)
Assess for illicit opioid use or injection drug use most or all the time ***	84 (77.1)
Clinician Practice, mean (SD)	
Years working with HIV patients	9 (8)
Hours/week patient care	35 (12)
Percent time HIV patient care	45 (37)
Number of direct care HIV patients	155 (173)

* Missing 1 clinician's response, n = 118

** > 10% patients treated with chronic or acute opioids, have OUD or are using injection drugs, 7 missing responses

*** 10 missing responses

Abbreviations: Standard deviation- SD

Table 2:

Post vs pre-intervention Adjusted Odds Ratios (AOR) of clinic-level and clinician buprenorphine prescribing using EMR and survey data

	AOR (95% CI)	p value
Patient with HIV prescribed buprenorphine	1.47 (0.50–4.28)	0.49
At least one in-site clinician prescribing buprenorphine	3.09 (0.54 – 18.00)	0.21
Self-reported buprenorphine prescribing	1.63 (0.78–3.41)	0.20
Self-reported completing buprenorphine waiver training	2.54 (1.38, 4.68)	0.01
Self-reported obtained DEA waiver	2.11 (1.12, 3.95)	0.02

Abbreviations: Confidence Interval- CI; Drug Enforcement Administration- DEA; Adjusted Odds ratio- AOR; Electronic medical record, EMR

Table 3:

Post vs pre-intervention attitudes towards prescribing buprenorphine among HIV clinicians (0 – 100 scale)

	Baseline Mean +/− SD	6 month follow-up Mean +/− SD	12 month follow-up Mean +/− SD	Mean Change (95% CI)	p value
Interest	65.0 (34.1)	65.8 (34.3)	65.8 (34.5)	−2.52 (−12.73, 7.70)	0.63
Confidence	43.6 (36.1)	54.7 (34.7)	57.6 (34.2)	12.27 (0.69, 23.84)	0.04
Readiness	44.5 (36.9)	55.4 (36.1)	57.3 (37.4)	10.89 (−0.31, 22.09)	0.06
Commitment	59.9 (35.5)	63.4 (34.6)	62.6 (36.1)	1.31 (−9.90, 12.52)	0.82

Clinicians' attitudes of interest, confidence, readiness, and commitment to prescribe buprenorphine were measured using 0–100 visual analog scale change readiness rulers (0: Not at all – 100: Extremely). Pre-post intervention mean change in measure is shown via model results.

Abbreviations: Confidence Interval- CI, Standard deviation- SD