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Buprenorphine physician–pharmacist collaboration in the management of patients with opioid use disorder: results from a multisite study of the National Drug Abuse Treatment Clinical Trials Network

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ABSTRACT

Background and Aims Physician and pharmacist collaboration may help address the shortage of buprenorphine-waivered physicians and improve care for patients with opioid use disorder (OUD). This study investigated the feasibility and acceptability of a new collaborative care model involving buprenorphine-waivered physicians and community pharmacists. **Design** Nonrandomized, single-arm, open-label feasibility trial. **Setting** Three office-based buprenorphine treatment (OBBT) clinics and three community pharmacies in the United States. **Participants** Six physicians, six pharmacists, and 71 patients aged ≥18 years with Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) OUD on buprenorphine maintenance. **Intervention** After screening, eligible patients' buprenorphine care was transferred from their OBBT physician to a community pharmacist for 6 months. **Measurements** Primary outcomes included recruitment, treatment retention and adherence, and opioid use. Secondary outcomes were intervention fidelity, pharmacists' use of prescription drug monitoring program (PDMP), participant safety, and satisfaction with treatment delivery. **Findings** A high proportion (93.4%, 71/76) of eligible participants enrolled into the study. There were high rates of treatment retention (88.7%) and adherence (95.3%) at the end of the study. The proportion of opioid-positive urine drug screens (UDSs) among complete cases (i.e. those with all six UDSs collected during 6 months) at month 6 was (4.9%, 3/61). Intervention fidelity was excellent. Pharmacists used PDMP at 96.8% of visits. There were no opioid-related safety events. Over 90% of patients endorsed that they were "very satisfied with their experience and the quality of treatment offered," that "treatment transfer from physician's office to the pharmacy was not difficult at all," and that "holding buprenorphine visits at the same place the medication is dispensed was very or extremely useful/convenient." Similarly, positive ratings of satisfaction were found among physicians/pharmacists. **Conclusions** A collaborative care model for people with opioid use disorder that involves buprenorphine-waivered physicians and community pharmacists appears to be feasible to operate in the United States and have high acceptability to patients.

Keywords Buprenorphine collaborative care, office-based buprenorphine treatment, opioid use disorder, pharmacist-provided care, primary care, pharmacy practice.

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INTRODUCTION

The vast majority of individuals with opioid use disorder (OUD) do not receive OUD treatment in the United States (US) [1,2]. Expanding access to office-based buprenorphine treatment (OBBT) addresses the OUD treatment gap and reduces opioid-related morbidity [3]. The US Drug Addiction Treatment Act (DATA) of 2000 allows office-based,

primary care physicians to apply for a waiver to prescribe buprenorphine for expanding OUD treatment outside of an opioid treatment program [4]. However, less than 10% of US primary care providers are buprenorphine-waivered prescribers [1]. Among buprenorphine-prescribing physicians, a range of practice has been observed; fewer than 10% treated over 75 patients, whereas ~20% treated only 1 to 3 patients [5]. Provider capacity and treatment access barriers could be addressed by pharmacists. Pharmacists are medication experts and natural partners for prescribers in team-based care. They dispense prescription medications, educate patients about safe medication practices, and could be trained to identify red flags for intervention (e.g. diversion, improper prescribing), provide counseling, and help treatment referrals [6,7]. Pharmacists are among the most trusted healthcare professionals [8] and they are highly accessible, even in US rural areas with relatively high opioid death rates [9]. Approximately 90% of Americans live within 5 miles of a community pharmacy [10]; in contrast, almost 20 million US residents live in a county without a buprenorphine-waivered practitioner [11].

Physicians and pharmacists can collaborate to improve access to OBBT and thereby allow physicians time for other priorities (e.g. seeing more patients). For example, OBBT in France has been allowed since 1995, and physicians have collaborated with pharmacists to improve access to OBBT by enabling pharmacists to provide daily, supervised dosing of buprenorphine [12]. The majority of patients receiving OBBT in France see one prescriber and go to one pharmacy, and pharmacist-provided services for buprenorphine have contributed to expanded access to OBBT in France [12,13]. Pharmacists in the United States are underused resources for enhancing access to OBBT. The US opioid overdose epidemic has led to an increase in buprenorphine prescriptions filled (i.e. annual buprenorphine treatment per 1000 population: 1.97 in 2009 vs. 4.43 in 2018); however, rates of buprenorphine treatment remain below national estimates of rates of OUD [14]. Patients with OUD receiving care from a buprenorphine-waivered physician in the United States typically go to a pharmacy monthly to refill their buprenorphine prescriptions. This monthly visit to a pharmacy represents an opportunity to leverage pharmacists' expertise in medication therapy management. Collaboration between OBBT physicians and licensed community pharmacists to deliver buprenorphine management particularly to stabilized patients offers opportunities to expand OBBT access through a collaborative care provider multiplier approach.

Community pharmacists are an under-used and under-studied group of healthcare professionals for partnering with buprenorphine-waivered prescribers to improve treatment access. There has been only one report of a physician–pharmacist collaborative care model for buprenorphine treatment in the United States, which involved a pilot program of 12 patients with OUD at a suburban health department [15]. This pilot program reported positive results, including high treatment retention, enhanced communication between physicians and pharmacists, improved patient care and diversion monitoring, and reduced physician burdens. Research is needed to inform physician–pharmacist OBBT collaborative care model implementation, particularly involving community pharmacists (i.e. those not internal to OBBT clinics), and this aspect of design may confer greater external validity.

We conducted the first US pilot trial exploring feasibility and acceptability of a physician–pharmacist collaborative model that involved transitioning OBBT of patients with OUD from a physician care model to a collaborative care model incorporating community pharmacies. This study builds on a need to expand healthcare professional involvement in OBBT provision to both increase treatment access and address the opioid overdose epidemic [1,7,11,16,17].

METHODS

Setting

This study was conducted in three OBBT clinics, including one academic medical center outpatient clinic and two non-academic, private clinics in the Raleigh/Durham area, North Carolina. Each clinic had at least two buprenorphine-waivered physicians who partnered with a single, nearby community pharmacy employing at least two licensed pharmacists. Study activities were conducted within private spaces at each pharmacy (i.e. space used for private consultations, immunizations *etc.*). Six physicians from three clinics, six pharmacists from three community pharmacies, and 71 patients participated in the study.

Study design

Pharmacists first completed 6 one-hour training modules from the Providers' Clinical Support System for Medication Assisted Treatment (PCSS-MAT: https://pcssnow.org/) (i.e. epidemiology information about OUD, OUD diagnosis, and features of buprenorphine treatment), eight 1-hour face-to-face coaching meetings with study physicians to review/discuss OUD care and processes, and protocol-specific training (e.g. training slides about study design/procedures, case report forms and documentation, study manual of operations). Next, patients with OUD receiving a regular dose regimen of buprenorphine were identified by physician referral and self-referral from advertisements and recruited from OBBT clinics. After providing written informed consent and completing baseline assessments, participants had their monthly buprenorphine prescription and maintenance care transferred to the partnering pharmacy, and treatment was managed by pharmacists for 6 months. At the

end of the study, participants were referred back to the OBBT clinic for usual care. Participant recruitment occurred between March 14, 2018 and December 3, 2018. This study was approved by Duke University Health System Institutional Review Board (IRB) and registered at ClinicalTrials.gov (NCT03248947).

Participant eligibility

Adults meeting Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for OUD [18], who had been stabilized on buprenorphine (i.e. received the same dose for at least 3 weeks) and were currently in treatment for no more than 12 months at study sites, were contacted by research staff to pre-screen for eligibility (Supporting information Table S1). Individuals with serious medical, psychiatric, substance use disorder, or social circumstances that would increase safety concerns were excluded. Those who met eligibility criteria and were interested in participating then provided informed consent and completed baseline assessments. A similar number of participants were recruited from each OBBT clinic.

Study Intervention

We used an operational care agreement (OCA) to specify pharmacist-provided patient care roles and responsibilities during monthly pharmacy visits and to establish collaboration for three partnered clinic-pharmacy sites [19]. The OCA specified that buprenorphine-waivered physicians were responsible for reviewing patient assessments, prescribing buprenorphine, keeping records for Drug Enforcement Administration inspections, and providing clinical guidance and coaching/supervision to the pharmacist, as needed, for managing buprenorphine treatment and follow-up. Therefore, physicians no longer spent time in personal interaction with patients monthly, unless needed. At each monthly pharmacy visit, research staff administered study assessments to buprenorphine patients and documented opioid withdrawal (Clinical Opioid Withdrawal Scale [20]), opioid craving (visual analog craving scale [21]), substance use (urine drug screen [UDS] and timeline follow-back), counseling attendance, psychosocial problems, suicidality risk (P4 Screener [22] and PHQ-9 [23]), and safety events (e.g. emergency department [ED] visits, and hospitalizations). Results from assessments were summarized on a buprenorphine visit checklist (BVC), which was reviewed by the pharmacist and supervising physician before releasing the monthly buprenorphine prescription. Physicians also checked the prescription drug monitoring program (PDMP) for signs of diversion (e.g. multiple buprenorphine prescriptions, other opiate prescriptions), completed/updated patient's OUD treatment plan, prescribed buprenorphine, and documented their tasks completed on the BVC. The PDMP is an electronic database that tracks controlled substance prescriptions in a state to provide information about prescribing and patient behaviors [24]. Before dispensing buprenorphine, pharmacists also checked the PDMP for signs of diversion, performed medication/dose reconciliation, conducted patient education/counseling based on results on the BVC and PDMP findings (e.g. overdose prevention, medication use, safety storage of medications); which were designed to follow the physician's approach during the office visits. Finally, pharmacists confirmed negative urine pregnancy test results for female participants and documented their tasks completed on the BVC. Fig. 1 summarizes and compares usual care and the physician–pharmacist collaboration model.

Outcome assessments

Each participant was expected to attend 6 monthly pharmacy visits. Primary outcome measures included feasibility (recruitment, retention) and treatment outcomes (adherence, opioid/other substance use). Treatment retention was defined as the proportion of scheduled pharmacy visits completed at the end of the study. Medication adherence was defined as the proportion of participants who took their monthly prescribed buprenorphine measured by medication reconciliation conducted by the pharmacist at each monthly pharmacy visit. Opioid use was confirmed by positive UDS results for opioids, oxycodone, or methadone. Non-opioid substance use included positive UDS results for other substances (amphetamine, barbiturates, benzodiazepines, cocaine, ecstasy, marijuana, and methamphetamine). Protocol adherence by physicians and pharmacists was tracked using the BVC (i.e. one for each monthly pharmacy visit attended) (Table 3).

Secondary outcome assessments provided additional information about the feasibility and acceptability. Intervention fidelity was assessed by adherence to the BVC by research staff, physicians, and pharmacists at each monthly visit, which was measured by the number of items (tasks) completed on randomly sampled BVCs. Intervention fidelity was evaluated on 35.0% (142/406) of all BVC forms from all three partnered clinic-pharmacy sites. Protocol adherence was defined by the proportion of BVCs (visits) with ≥80% tasks completed [25]. Pharmacists' PDMP use included monitoring for multiple buprenorphine prescriptions and other class II and III medication prescriptions with a potential for misuse [26]. Participant, pharmacist, and physician satisfaction with treatment delivery was assessed using a self-administered, web-based treatment satisfaction survey (eight items) [27]. Participant safety measures included substance-related overdoses and substance-related ED visits or hospitalizations.

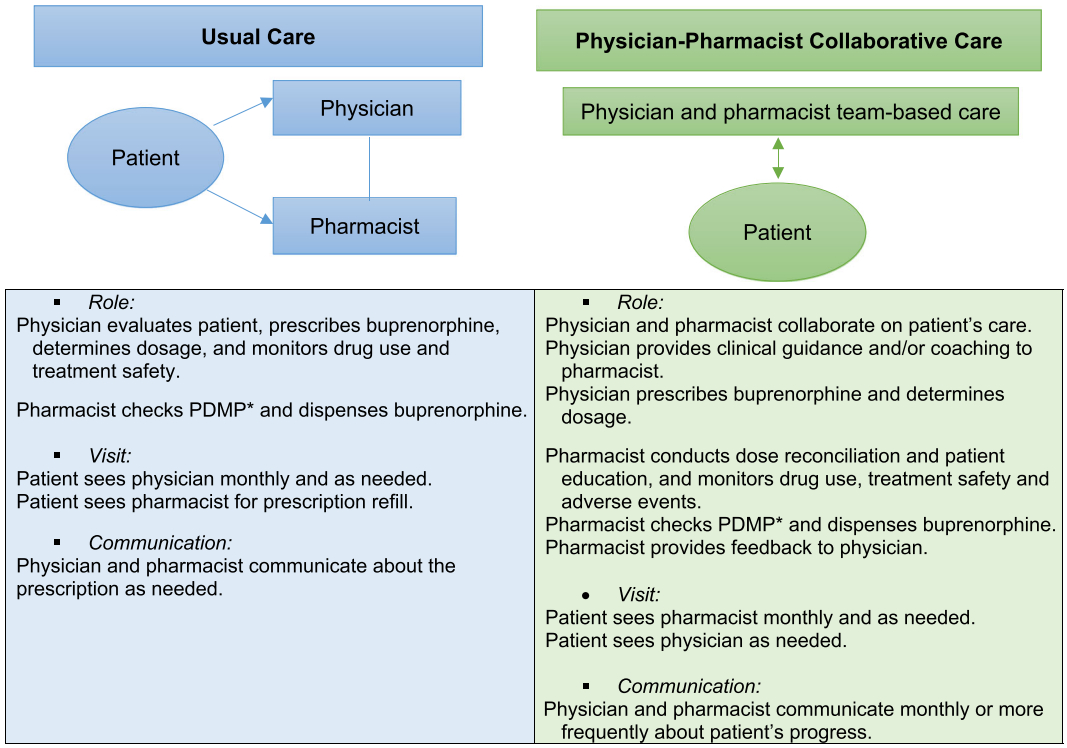


Figure 1 A summary of usual care and physician-pharmacist collaborative care model

Statistical analyses

Descriptive analyses were conducted to characterize distributions of outcome measures. The primary method of handling missing UDS was to impute missing as positive, and additional imputation methods were explored. Analyses were conducted in Statistical Analysis System (SAS) 9.4 [28].

RESULTS

Recruitment

Of the 96 adult patients approached, only four patients (4.2%) declined pre-screening (Fig. 2). Of these, 76 (82.6% of pre-screened) ultimately met criteria for study participation with the majority of those eligible (71/76) entering the maintenance phase to receive pharmacist-provided care.

Demographic characteristics at baseline

Of the 71 participants at baseline, the majority were men (60.6%), aged 18–44 years (71.8%), non-Hispanic (98.6%), white (85.9%), had some college or higher education (57.7%), and were employed (62.0%) (Table 1).

Treatment retention and medication adherence

As shown in Table 2, the overall study visit attendance rate during the 6-month phase was 95.3% (406/426 visits; 94.9–95.5% across sites), which was similar among men (95.7%, 247/258) and women (94.6%, 159/168). The treatment retention rate at month 6 was 88.7% (63/71), which was similar across sites (87.0–90.9%). Reasons for early termination ($n = 8$) varied across patients and are detailed in Fig. 2. During each month, 100% of those retained in the study met criteria for medication adherence.

Opioid use

At study entry, 8.5% of participants had a positive UDS for opioid use (4.5–13.0% across sites). There were a total of 18 missing UDS samples, ranging from 0 at month 1 to 7 at month 6. As shown in Fig. 3, proportions of opioid-positive UDS were steady at or under 5% across the 6-month study period for complete cases (i.e. those with all 6 UDSs collected during 6 months; n = 61) and under 9% for submitted samples (i.e. no imputation for missing UDS). Only when missing UDSs were imputed as positive did opioid detection rates rise above 10%.

Overall, monthly opioid-positive UDS was 9.9% (42/426 months) with missing UDS imputed as positive, 3.3% (12/366 months) for complete cases, 5.6% (24/426 months) for missing UDS imputed as negative,

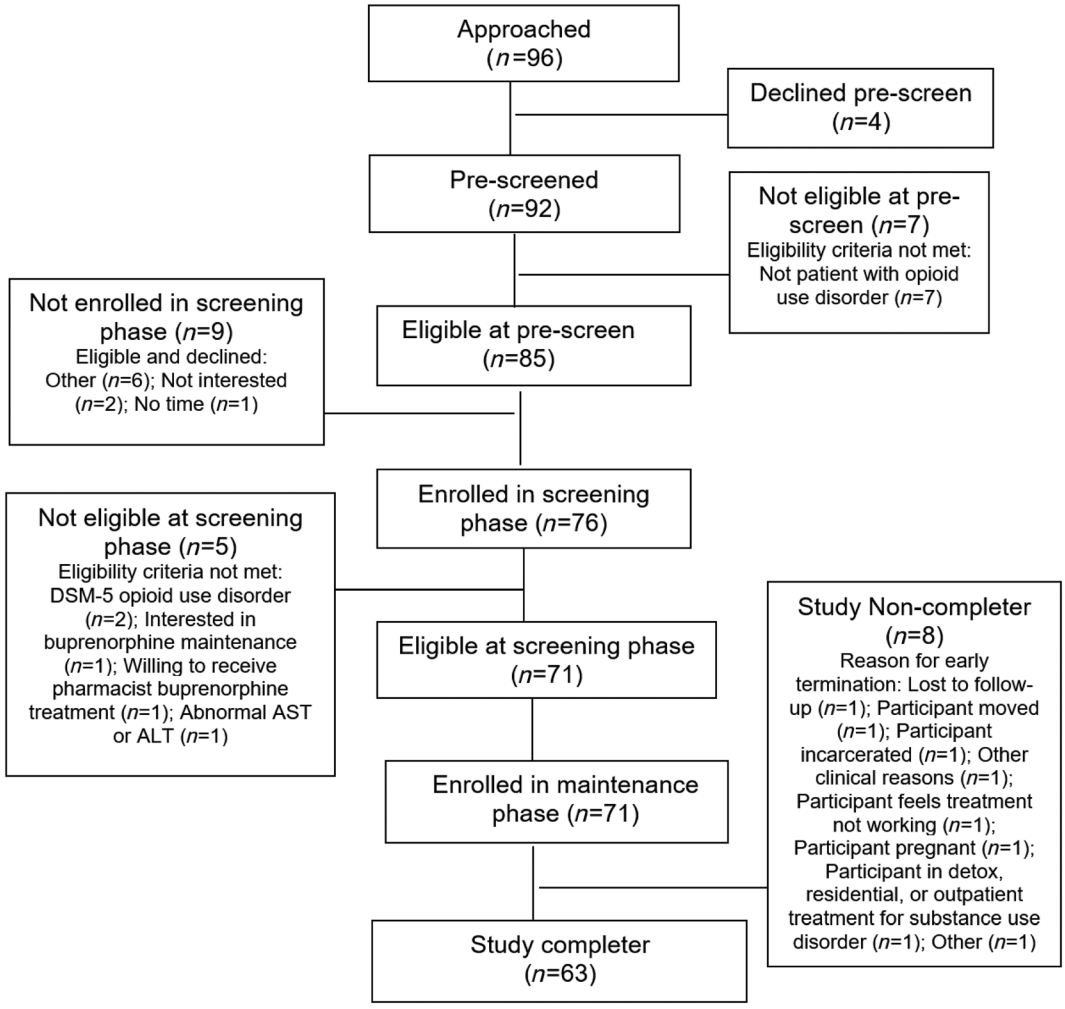


Figure 2 CONSORT flow diagram

and 5.9% (24/408 months) when no imputation was used (Supporting information Table S2).

Non-opioid substance use

The overall non-opioid positive UDS rate was 51.4% with missing UDS imputed as positive, 47.2% when missing UDS were imputed as negative, 46.4% in complete cases, and 49.3% with no imputation. Rates were virtually identical for men and women, and no significant monthly variation in prevalence of positive tests for non-opioid substances was noted across the 6-month period.

At screening/intake, the most commonly used non-opioid drugs were cannabis (32.4%, 23/71) and non-prescribed benzodiazepines (14.1%, 10/71). Prevalence of amphetamine, cocaine, and methamphetamine use was 7.0% (5/71), 5.6% (4/71), and 1.4% (1/71), respectively. The pattern of results was similar at Month 6 with 35.9% (23/64) for cannabis, 12.5% (8/64) for benzodiazepines, 6.3% (4/64) for amphetamines, 4.7% (3/64) for cocaine, and 4.7% (3/64) for methamphetamines.

Intervention fidelity

Fidelity was determined by counting the number of items/tasks on the BVC completed during each pharmacy visit (Table 3). We randomly evaluated 142 BVC forms (142/406) from all three partnered clinic-pharmacy sites, assessing a total of 2374 items. Only two tasks out of the 2374 items assessed were not completed (Supporting information Table S3). Proportion of visits showing ≥80% adherence to study visit tasks was 100% at each site.

Pharmacists' use of the PDMP

Pharmacists used the PDMP in 96.8% of the total visits (396/409 visits; Supporting information Table S4). The 409 visits included three visits because of early study termination. Of the 13 visits without PDMP use, the PDMP system was not working for 11 visits (the system was down, website not working). There were no multiple buprenorphine prescriptions, other opioid prescriptions,

Table 1 Participant characteristics at baseline

Characteristic	*Total (n = 71)*
Clinic site	
Site 1	26 (36.6%)
Site 2	22 (31.0%)
Site 3	23 (32.4%)
Sex	
Male	43 (60.6%)
Female	28 (39.4%)
Age (mean (SD))	38 (11.5)
Age in years	
18–44	51 (71.8%)
45–75	20 (28.2%)
Ethnicity	
Not Hispanic or Latino	70 (98.6%)
Hispanic or Latino	1 (1.4%)
Race	
White	61 (85.9%)
Non-white	10 (14.1%)
Education completed	
High school graduate/GED or less	30 (42.3%)
Some college or more	41 (57.7%)
Marital status	
Married/living with partner	22 (31.0%)
Widowed/divorced/separated	21 (29.6%)
Never married	28 (39.4%)
Employment	
Working now	44 (62.0%)
Not working/other	27 (38.0%)
Number of positive urine drug screens for opioids at screening	6 (8.5%)

or unauthorized benzodiazepine or other controlled medication use reported for 98.5% of visits where the PDMP was consulted.

Safety monitoring

There were no substance-related overdose events. There was one substance-related ED visit (muscle cramping associated with cocaine use), one substance-related hospitalization (e-cigarette skin burn), and one pregnancy (live birth outcome: vaginal delivery/healthy infant) reported during the study.

Treatment delivery satisfaction in participants

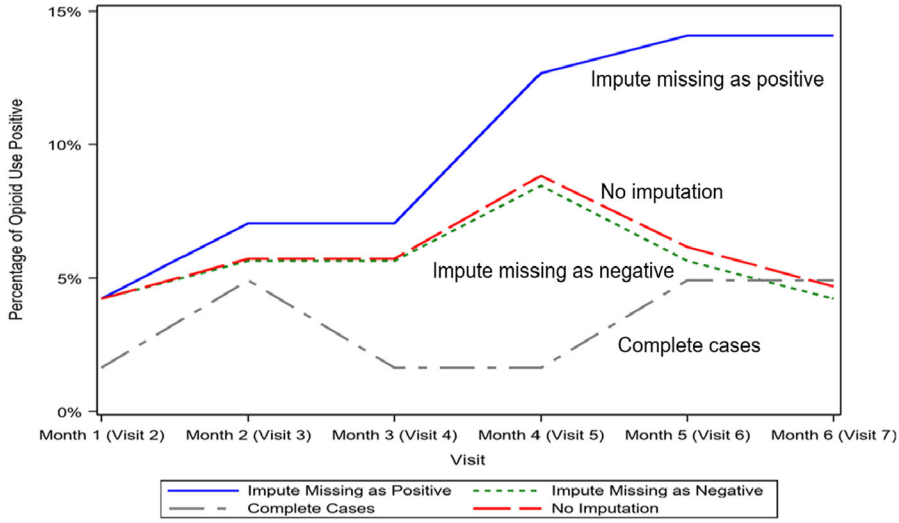
Sixty-three participants completed the satisfaction survey at Month 6 (Table 4), comprising all who remained in the study for 6 months. Among them, 98.4% were either satisfied (4.8%) or very satisfied (93.7%) with their overall experience in this study; 98.4% were either satisfied (7.9%) or very satisfied (90.5%) with the quality of treatment offered in this study; 96.8% reported that treatment transfer from physician's office to the pharmacy was not difficult at all; 95.2% reported that holding the buprenorphine visits at the same place the medication is dispensed (i.e. at the pharmacy) was either extremely useful/convenient (82.5%) or very useful/convenient (12.7%); 98.4% endorsed that they would definitely choose to participate in the study again if given the opportunity. Reasons for influencing participants' decision to participate in a future study were: "My participation may help to improve and expand treatment delivery/options" (100%); "Pharmacy is the right location for this type of treatment" (96.8%); "The treatment offered (i.e. physician–pharmacist collaborative care) was of better quality than the usual treatment" (85.7%); and "It was easy to understand/distinguish patient, physician, and pharmacist roles" (96.8%).

The survey also asked participants to assess effectiveness of the physician–pharmacist collaborative care model compared to the care they had before the study. The majority reported the physician–pharmacist collaboration model to be "more effective" with regard to (i) having more than one health professional figure involved (58.7%), (ii) time spent in each visit (65.1%), (iii) time to release buprenorphine prescription (69.8%), and (iv) efficiency of treatment delivery (81.0%).

Table 2 Medication visit adherence

	Total (n = 71)	*Male (n = 43)*	*Female (n = 28)*
Medication adherence[a]			
Month 1 (%)	71/71 (100.0)	43/43 (100.0)	28/28 (100.0)
Month 2 (%)	70/71 (98.6)	43/43 (100.0)	27/28 (96.4)
Month 3 (%)	70/71 (98.6)	42/43 (97.7)	28/28 (100.0)
Month 4 (%)	69/71 (97.2)	41/43 (95.3)	28/28 (100.0)
Month 5 (%)	63/71 (88.7)	39/43 (90.7)	24/28 (85.7)
Month 6 (%)	63/71 (88.7)	39/43 (90.7)	24/28 (85.7)
Overall[b]	406/426 (95.3)	247/258 (95.7)	159/168 (94.6)

[a]Participants who took any of the dispensed study medication during the month were considered adherent for the study visit. [b]Early termination visits are not included (n = 2 for total, *n* = 1 for male, n = 1 for female).



Note: The number of missing UDS samples at each month: Month 1 (*n*=0), Month 2 (*n*=1), Month 3 (*n*=1), Month 4 (*n*=3), Month 5 (*n*=6), and Month 6 (*n*=7). Complete cases was defined as those with all 6 UDSs collected during the 6-month maintenance phase (*n*=61). Positive UDS results at Month 6: complete cases (3/61, 4.9%), no imputation (3/64, 4.7%), impute missing as negative (3/71, 4.2%), and impute missing as positive (10/71, 14.1%). At Month 5, only 4 of the opioid-positive participants provided a urine sample, and the other 6 opioid-positive participants were only positive due to imputation (early termination). At Month 6, only 3 participants provided an opioid-positive urine sample, and the other 7 participants required imputation as opioid-positive.

Figure 3 Opioid-positive urine drug screen (UDS) results during the maintenance phase with various imputation methods

Table 3 Summary of tasks for physicians and pharmacists on the Buprenorphine Visit Checklist

Tasks/Items	*Physician*	*Pharmacist*
Opioid withdrawal, per Clinical Opioid Withdrawal Scale (COWS)[a]	x	x
Self-reported opioid craving, per Visual Analog Scale (VAS)[a]	x	x
Urine drug testing[a]	x	x
Self-reported substance use (timeline follow-back)[a]	x	x
Psychosocial counseling attendance[a]	x	x
Problem list (substance use, financial, family, social, psychiatric, legal, or medical issues)[a]	x	x
Suicidality assessment[a]	x	x
Concomitant medication treatment/medication list (e.g. taking any new prescription drugs since the last visit)[a]	x	x
Safety event response checklist (e.g. hospitalizations, overdose events, emergency department visits, deaths)[a]	x	x
Check state prescription drug monitoring program	x	x
Treatment plan for opioid use disorder	x	
Buprenorphine dose adjustment	x	
Buprenorphine prescribing	x	
Medication reconciliation (buprenorphine film count)		x
Patient education (e.g. overdose prevention, other drug use, compliance with psychosocial treatment and medications, safety storage of medications)		x
Urine pregnancy test (i.e. female participant provided a negative urine pregnancy test before buprenorphine dispensing)		x
Buprenorphine dispensing		x

[a]Research coordinator completed data collection for each monthly visit before the pharmacist saw the participant. The pharmacist monitored/recorded the information for each task and added progress notes or comments to communicate the feedback with the physician at each monthly visit. The physician also monitored the information and recorded progress notes or comments on the Buprenorphine Visit Checklist, and communicated with the pharmacist remotely at each monthly pharmacy visit (e.g. dose adjustment, concerns with drug use).

Treatment delivery satisfaction in physicians and pharmacists

All six physicians and six pharmacists completed satisfaction surveys at the end of the study (Table 5). Of them (n = 12), 100% reported being very satisfied with their overall experience in this study; 100% were either very satisfied (91.7%) or satisfied (8.3%) with the quality of treatment offered in this study; 83.3% reported that treatment transfer from physician's office to the pharmacy

Table 4 Treatment delivery satisfaction in participants at Month 6 ($n = 63$)

Questions	*Percent*
Overall, how satisfied are you with your experience in this study?	
Very satisfied	93.7
Satisfied	4.8
Neither satisfied nor dissatisfied	0
Dissatisfied	1.6
Very dissatisfied	0
Overall, how satisfied are you with the quality of treatment offered in this study?	
Very satisfied	90.5
Satisfied	7.9
Neither satisfied nor dissatisfied	0
Dissatisfied	1.6
Very dissatisfied	0
How difficult do you think it made it for the treatment to be transferred from the physician's office to the pharmacy?	
Not difficult at all	96.8
Somewhat difficult	1.6
Very difficult	0
Extremely difficult	1.6
How useful/convenient do you think it is to hold buprenorphine visits in the same place the medication is dispensed?	
Not at all useful/convenient	0
Somewhat useful/convenient	1.6
Moderately useful/convenient	3.2
Very useful/convenient	12.7
Extremely useful/convenient	82.5
How effective did you find the following aspects of the study?	
Having more than one health professional figure involved?	
Less effective	3.2
No difference in effectiveness	38.1
More effective	58.7
Time spent in each visit	
Less effective	4.8
No difference in effectiveness	30.2
More effective	65.1
Time to release buprenorphine prescription	
Less effective	6.3
No difference in effectiveness	23.8
More effective	69.8
Efficiency of treatment delivery	
Less effective	1.6
No difference in effectiveness	17.5
More effective	81.0
If you had to do it all over again, would you still choose to participate in the study?	
Definitely participate	98.4
Probably participate	1.6
Probably not participate	0
Definitely not participate	0
Indicate whether each of the following would influence your decision to participate again	
My participation may help to improve and expand treatment delivery/options	
No	0
Yes	100.0
Pharmacy is the right location for this type of treatment	
No	3.2
Yes	96.8
The treatment offered was of better quality than the usual treatment	
No	14.3
Yes	85.7
It was easy to understand/distinguish patient, physician, and pharmacist roles	
No	3.2
Yes	96.8

(***Continues***)

Table 4. (Continued)

was not difficult at all; 100% reported that holding the buprenorphine visits at the same place the medication is dispensed was either very (25%) or extremely useful/convenient (75%); 100% endorsed that they would choose to participate in the study if given the opportunity. Reasons for influencing their decision to participate in a future study were: "My participation may help to improve and expand treatment delivery/options" (100%); "Pharmacy is the right location for this type of treatment" (91.7%); "The treatment offered (physician–pharmacist collaborative care) was of better quality than the usual treatment" (58.3%); and "It was easy to understand/distinguish patient, physician, and pharmacist roles" (91.7%).

Physicians and pharmacists were also asked about collaborative care model effectiveness. The majority reported the model to be "more effective" with regard to (i) having more than one health professional figure involved (75.0%), (ii) time spent in each visit (83.3%), (iii) time to release buprenorphine prescription (75.0%) and (iv) efficiency of treatment delivery (66.7%).

DISCUSSION

These findings support engagement of community pharmacists in OUD treatment and research [7]. This study was not conducted using pharmacies internal to clinics, but involved non-academic community pharmacies coupled with three distinct OBBT clinics. Although all pharmacies were research naïve sites, there was no retention or operational issues, which highlight the feasibility of a physician–pharmacist collaboration model. High rates of 6-month patient retention (88.7%) and medication visit adherence (95.3%) observed supports the feasibility,

Table 5 Treatment delivery satisfaction in physicians and pharmacists at the end of the study (n = 12)

Question	*Percent*
Overall, how satisfied are you with your experience in this study?	
Very satisfied	100.0
Satisfied	0
Neither satisfied nor dissatisfied	0
Dissatisfied	0
Very dissatisfied	0
Overall, how satisfied are you with the quality of treatment offered in this study?	
Very satisfied	91.7
Satisfied	8.3
Neither satisfied nor dissatisfied	0
Dissatisfied	0
Very dissatisfied	0
How difficult do you think it made it for the treatment to be transferred from the physician's office to the pharmacy?	
Not difficult at all	83.3
Somewhat difficult	16.7
Very difficult	0
Extremely difficult	0
How useful/convenient do you think it is to hold buprenorphine visits in the same place the medication is dispensed?	
Not at all useful/convenient	0
Somewhat useful/convenient	0
Moderately useful/convenient	0
Very useful/convenient	25.0
Extremely useful/convenient	75.0
How effective did you find the following aspects of the study?	
Having more than one health professional figure involved	
Less effective	0
No difference in effectiveness	25.0
More effective	75.0
Time spent in each visit	
Less effective	0
No difference in effectiveness	16.7
More effective	83.3
Time to release buprenorphine prescription	
Less effective	8.3
No difference in effectiveness	16.7
More effective	75.0
Efficiency of treatment delivery	
Less effective	0
No difference in effectiveness	33.3
More effective	66.7
If you had to do it all over again, would you still choose to participate in the study?	
Definitely participate	100.0
Probably participate	0
Probably not participate	0
Definitely not participate	0
Indicate whether each of the following would influence your decision to participate again	
My participation may help to improve and expand treatment delivery/options	
No	0
Yes	100.0
Pharmacy is the right location for this type of treatment	
No	8.3
Yes	91.7
The treatment offered was of better quality than the usual treatment	
No	41.7
Yes	58.3
It was easy to understand/distinguish patient, physician, and pharmacist roles	
No	8.3
Yes	91.7

acceptability, and potential effectiveness of the model. Of note, pharmacists' study activities were not limited to dispensing buprenorphine, but also included evaluation/counseling of patients regarding psychosocial problems and their detected drug use, as well as frequent communication with study physicians regarding the PDMP findings, safety events, and buprenorphine dosing adjustment. These aspects further support the feasibility of future trial conduct and implementation of pharmacist-provided OUD care [7, 29].

This is the first trial in the United States studying the feasibility and acceptability of physician–pharmacist collaboration in managing OBBT for OUD. Our results indicate successful attainment of feasibility and acceptability regarding recruitment, recruitment rate, treatment retention/adherence, intervention fidelity, pharmacists' use of the PDMP, participant safety, and satisfaction with treatment delivery. At month 6, only three retained patients had an opioid-positive UDS. These results provide support that has otherwise been lacking to guide implementation of pharmacist-provided care for OUD, as encouraged by several professional organizations. For instance, American Pharmacists Association (APhA) published a statement to advocate for the essential role of pharmacists in addressing opioid misuse, addiction, and diversion [6]. The Association for Multidisciplinary Education and Research in Substance Use and Addiction (AMERSA) has developed core competencies for pharmacists to address substance use in the 21st century and sustain their collaborative role in addiction care, such as managing OBBT for OUD [7].

In addition, one major issue that impedes current efforts addressing the opioid overdose epidemic is a limited number of OBBT practitioners and uneven distributions with fewer providers in rural areas [1,11], which is complicated by the national crisis of physician shortage and

burnout [16]. By 2030, it is estimated to be a shortfall of up to 55 200 primary care providers and a shortage of up to 65 800 specialty physicians in the United States [30]. The physician–pharmacist collaborative model tested in this trial was defined by an OCA [19], which incorporated evidence-based care for OBBT into the regular scope of community pharmacy practices to fit into what pharmacists are already doing or are prepared to do [6,31,32]. This integrated care model has the potential to address the shortage of OBBT practitioners by increasing OBBT providers' capacity to accept new patients [17].

There were no opioid-related ED visits/hospitalizations, study-related safety concerns, or retention issues with physicians/pharmacists during the 6-month care at the pharmacy. Even though the state of North Carolina does not require pharmacists to check the PDMP for every controlled medication prescription, we found consistent use of the PDMP by pharmacists and no signs of diversion from patients. UDS results showed no worsening of opioid or other drug use. Nearly all patients were satisfied with the quality of treatment offered, endorsing pharmacies as ideal settings for treatment receipt. Physicians/pharmacists reported similar positive findings. Because satisfaction data were collected by self-administration using a computer, "perceived bias" of responding positively to questions because of presence of research staff was reduced. Most patients and physicians/pharmacists also reported improved efficiency of care regarding time spent in each visit and waiting time to receive buprenorphine prescription by including a pharmacist involved with treatment delivery. Moreover, the majority of patients, physicians, and pharmacists reported that physician–pharmacist collaborative care was of better quality than usual OBBT for OUD. These findings support acceptability of physician–pharmacist collaboration from perspective of patients, physicians, and pharmacists.

Limitations

Although this pilot study was not a randomized trial, it was intended to explore the feasibility and acceptability of recruitment and implementation of physician–pharmacist collaboration at different OBBT settings and new research settings (i.e. pharmacies). This study was restricted to community OBBT clinics and community pharmacies in North Carolina. Participants were a convenience sample of patients. This study was limited in that research staff provided assessment information about patient status to practitioners, which would not be available in a true real-world application. Additional studies are needed to test the model in different settings/locations, particularly rural areas, and to compare physicians and pharmacists on outcomes given their differences in training and responsibilities. Nonetheless, the main intent of this trial was to understand applicability of the physician–pharmacist collaborative model to an office-based setting.

CONCLUSIONS

Overall success of this pilot trial offers strong support for a physician–pharmacist collaborative care model to help improve buprenorphine treatment access for OUD. Future randomized trials are needed to test the efficacy, effectiveness, and implementation of physician–pharmacist collaborative care models for management and treatment of patients with OUD as part of real-world practice.

Clinical trial registration

ClinicalTrials.gov Identifier: NCT03248947

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Declaration of interests

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Author contributions

Li-Tzy Wu: Conceptualization; formal analysis; funding acquisition; investigation; methodology; project administration; resources; supervision. **William S. John:** Data curation; investigation; project administration. **Udi E. Ghitza:** Investigation; methodology; supervision. **Aimee Wahle:** Formal analysis; investigation; methodology. **Abigail G. Matthews:** Formal analysis; investigation; methodology. **Mitra Lewis:** Investigation. **Brett Hart:** Investigation; methodology. **Zach Hubbard:** Data curation. **Lynn A. Bowlby:** Investigation. **Lawrence H. Greenblatt:** Investigation. **Paolo Mannelli:** Conceptualization; formal analysis; funding acquisition; investigation; methodology; project administration; supervision.

Ethics and approvals

This work has been approved by the Duke University Health System IRB.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. The study inclusion and exclusion criteria
Table S2. Summary of opioid-positive urine drug screen (UDS) during the maintenance phase with various imputation methods
Table S3. Intervention fidelity based on the number of items completed on Buprenorphine Visit Checklist (BVC)
Table S4. Pharmacist use of the prescription drug monitoring program (PDMP)

