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PERSPECTIVES ON EMERGENCY DEPARTMENT-INITIATED
BUPRENORPHINE AMONG CLINICAL PHARMACISTS

A Thesis Submitted to the Yale University School of Medicine in Partial Fulfillment of
the Requirements for the Degree of Doctor of Medicine

By

Marissa Justen 2023

PERSPECTIVES ON EMERGENCY DEPARTMENT-INITIATED BUPRENORPHINE AMONG CLINICAL PHARMACISTS.

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Clinical pharmacists are well positioned to enhance efforts to promote Emergency Department (ED)-initiated buprenorphine to treat opioid use disorder (OUD). Among clinical pharmacists in urban EDs, we sought to characterize barriers and facilitators for ED-initiated buprenorphine to inform future implementation efforts and enhance access to this highly effective OUD treatment.

This study was conducted as a part of Project ED Health (CTN-0069, NCT03023930), a multisite effectiveness-implementation study aimed at promoting ED-initiated buprenorphine that was conducted between April 2017 and July 2020. Data collection and analysis were grounded in the Promoting Action on Research Implementation in Health Services (PARIHS) framework to assess perspectives on the relationship between 3 elements: **evidence** for buprenorphine initiation, the ED **context**, and **facilitation** needs to promote ED-initiated buprenorphine. Using content analysis, an iterative coding process was used to identify overlapping themes within these 3 domains.

Eight focus groups/interviews were conducted across four geographically disparate EDs with 15 pharmacist participants. Six themes were identified. Themes related to evidence included (1) varied levels of comfort and experience among pharmacists with ED-

initiated buprenorphine that increased over time and (2) a perception that patients with OUD have unique challenges that require guidance to optimize ED care. Regarding the context, clinical pharmacists identified: (3) their ability to clarify scope of ED care in the context of unique pharmacology, formulations, and regulations of buprenorphine to ED staff, and that (4) their presence promotes successful program implementation and quality improvement. Participants identified facilitation needs including: (5) training to promote practice change and (6) ways to leverage already existing pharmacy resources outside of the ED.

Clinical pharmacists play a unique and critical role in the efforts to promote ED-initiated buprenorphine. We identified 6 themes that can inform pharmacist-specific interventions that could aid in the successful implementation of this practice.

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1. Introduction

Recent provisional data from the Center for Disease Control (CDC) National Center for Health Statistics estimates that there were over 100,000 overdose-related deaths in the United States during the 12 month period ending in April 2021, a 28.5% increase from the year prior, and a nine-fold increase since the beginning of the opioid epidemic in the 1990s.^{1,2} These deaths pose as a significant public health concern, as exemplified by the fact that there were 1.68 million person-years of life lost in 2016 alone as a result of deaths attributed to opioid use.³

FDA approved medications for opioid use disorder (MOUD), including buprenorphine and methadone, are associated with reduced morbidity and mortality for individuals with OUD.⁴⁻⁸ Used together with psychotherapy, these medications are considered the standard of treatment for opioid use disorder. Such treatment can reduce opioid use, curb cravings, and treat withdrawal symptoms.⁹ MOUD can also improve retention in treatment, and can decrease risk of HIV and Hepatitis C transmission.¹⁰ Despite their proven efficacy, only 27.8% of individuals with opioid use disorder receive these medications.¹¹

Methadone is a full opioid agonist that was approved by the FDA as a treatment for OUD in 1972.¹² Based on reports of diversion and problematic use, the Drug Enforcement Administration designated methadone as a Schedule II substance in 1974.¹² Despite its designation as a Schedule II substance, the FDA's desire to create a "closed system of distribution" of methadone led to a five tier system of regulation that severely limits

provision of methadone and requires direct oversight and frequent toxicology screens.¹³ Because methadone can only be dispensed from one of the 1,500 designated methadone treatment centers, drive times, waitlists, and limited hours within these centers severely limit access to this medication.¹⁴ Moreover, while uncommon, methadone can also lead to sedation and respiratory depression.¹⁵

Buprenorphine, on the other hand, is a partial opioid agonist that was FDA approved in 2002, that can be delivered sublingually, through an injection, or implant. As a partial agonist, its unique pharmacology leads to a lower risk for respiratory depression and overdose when compared to methadone, while effectively reducing withdrawal symptoms and craving associated with OUD.¹⁶ The Drug Addiction Treatment Act (DATA) of 2000 allowed physicians to prescribe buprenorphine from an outpatient setting after obtaining an eight hour certification. In contrast to methadone, pharmacies can dispense buprenorphine for the treatment of OUD, allowing the integration of OUD treatment within general health settings including primary care offices, hospitals and emergency departments. In April of 2021, educational requirements were removed by the US federal government for clinicians who prescribed buprenorphine to under 30 patients, leading to a modest growth in the number of clinicians with buprenorphine waivers¹⁷ and on December 29, 2022, the “DATA-Waiver Program” was eliminated entirely by the Consolidated Appropriations Act of 2023. Moving forward, buprenorphine can be prescribed to treat OUD by all clinicians with a valid DEA waiver.¹⁸

Because many individuals with OUD within the US interface with the healthcare system through the Emergency Department, it is an excellent setting to initiate buprenorphine. In 2015, a landmark clinical trial evaluated the efficacy of brief intervention, initiation of buprenorphine, and referral to follow up care within the ED when compared to referral alone, and brief intervention and referral alone. Patients with OUD who were randomized to receive ED-initiated buprenorphine with primary care follow-up were twice as likely to be engaged in treatment at 30 days than those receiving a referral only or a brief intervention with a facilitated referral to OUD treatment.¹⁹ As a result of this study, the ED has emerged as a critical setting to initiate buprenorphine,²⁰ and while ED-initiated buprenorphine has been increasing among ED clinicians over the last decade,²¹ it continues to be underutilized within this setting.⁷ Additionally, despite this increase, notable sex, age, and racial disparities among recipients of ED-initiated buprenorphine continue to persist.²²

To optimize adoption and sustainability of ED-initiated buprenorphine, there has been growing recognition of the importance of multidisciplinary treatment teams including the involvement of clinical pharmacists. Broadly, clinical pharmacists have contributed extensively to the care of patients with substance use disorders. For example, within patients with alcohol use disorder (AUD), clinical pharmacists can provide patient education surrounding medications for AUD, provide recommendations for titration and monitoring frequency for prescribers, and carry out intramuscular naltrexone injections in some states.²³ Clinical pharmacists can also help to promote smoking cessation through optimization of nicotine replacement therapy and delivery of smoking cessation

counseling, and have been shown to improve abstinence rates for patients who chose to engage in such treatment modalities.^{10,24} Additionally, they can assist in the prevention and treatment of patients with OUD through monitoring opioid prescribing practices, pharmacy-based harm reduction efforts such as naloxone distribution and needle exchange programs, and assistance in the dispensation of MOUD in healthcare settings.^{25,26} Notably, a correspondence from the New England Journal of Medicine published on January 12, 2023 introduced a phase 3 randomized controlled trial held at 6 sites that compared pharmacy-based buprenorphine follow-up to provider-based usual care. This pilot study showed that “retention in pharmacy-based care was substantially higher than retention in usual care”.²⁷

In the ED, clinical pharmacists play a critical role in ensuring that patients’ medication needs are met through dissemination of medication information to medical providers, contribution to resuscitation efforts, involvement in delivery of high-alert medications, medication procurement and preparation, medication reconciliation, documentation, and transitions of care.²⁸ Pharmacists also have vital administrative responsibilities as exemplified by their involvement in quality improvement projects, interdisciplinary education efforts, and ED-based research and scholarly activity.²⁸ Additionally, the 2020 report by the American Society of Health-System Pharmacists identifies “providing structure to opioid crisis services” as a potential area for further emergency medicine pharmacist collaboration.²⁸ Because of this, clinical pharmacists are well positioned to influence the adoption of new clinical practices, including ED-initiated buprenorphine.

However, despite this positioning, our team has found that attitudes towards buprenorphine initiation are highly variable among non-pharmacist ED clinicians including attending physicians, residents, physician associates, and nurse practitioners. This variability results of lack of training and understanding of the evidence among clinicians, absence of protocol and referral networks within the ED, and continued existence of misconceptions and stigma surrounding possibilities of diversion of the medication.²⁹

Statement of Purpose

Because of such gaps in uptake of this practice, and the critical role of clinical pharmacists in EDs, we sought to characterize the perceived barriers and facilitators to ED-initiated buprenorphine among ED pharmacists in four urban, academic EDs across the United States. With such efforts, we aimed to improve delivery of MOUD by identifying opportunities for multidisciplinary collaboration involving ED pharmacists in the process of ED-initiated buprenorphine.

2. Methods

2.1 Overview of Project ED Health

Our investigation is part of a larger study, Project ED Health, a National Institute on Drug Abuse Clinical Trials Network funded effectiveness-implementation trial conducted between April 2017 and July 2020. This project aimed at evaluating the effect of Implementation-Facilitation (IF) strategies to promote the uptake of ED-initiated

buprenorphine with referral to ongoing MOUD treatment in four urban, academic EDs.³⁰
The study was approved by Western Institutional Review Board.

We grounded our interview guide and analysis in the Promoting Action on Research and Implementation Health Services (PARIHS) framework.³¹ This framework focuses on successful implementation of a particular clinical practice as being impacted by the dynamic relationship between three elements: Evidence, Context, and Facilitation. More specifically, evidence includes stakeholder perception of research, clinical experience, patient experiences, and local data related to the implementation of the evidence-based practice of ED-initiated buprenorphine. Context is used to refer to the leadership and culture within the setting in which the intervention is to be implemented. Facilitation refers to the processes necessary to implement the evidence-based practice. A Rapid Assessment Process among researchers was iteratively conducted throughout the study, in which fieldnotes from focus groups and stakeholder meetings were reviewed as a team and organized into matrices used to inform external IF activities.³²

2.2 Study Design and Setting

2.2.1 Selection of Participants: We conducted in-depth, semi-structured focus groups and interviews with ED clinical pharmacists who were eligible to participate in the provision of ED-initiated buprenorphine. Clinical pharmacists that worked in the ED and had been employed by their respective hospitals for at least six months prior to study onset. For this project, focus groups and interviews were conducted at four large academic, urban EDs in Baltimore, Maryland, New York City, New York, Cincinnati,

Ohio, and Seattle, Washington during a baseline evaluation period before IF, during the IF period, and during a post-IF evaluation period. Participants were recruited by research staff. Snacks were offered but no financial compensation was provided.

2.2.2 Data Collection and Measurements: Focus groups or interviews were conducted between April 2018 and July 2020 across 3 time points, corresponding to the baseline evaluation period (n=3), the IF period (n=2) and the post-IF evaluation period (n=3) (See Table A). In some cases (site B and site C), participants were not engaged across all three timepoints. Some participants may have participated in multiple focus groups across time points, but no identifying information was collected. Focus groups and interviews were facilitated by study authors (EJE, GD, DAF, PGO, KFH), who are emergency and internal medicine physicians with addiction medicine training from an outside institution. Group facilitators identified as both male and female and had training and experience in conducting qualitative research. There were no pre-existing relationships between facilitators and interviewees.

Focus groups and interviews were in-person, semi-structured, occurred in a non-clinical space and lasted 30 minutes to one hour. Facilitators used a previously published interview guide with prompts grounded in the PAHRIS framework.³⁰ Prompts were aimed at eliciting participant perspectives on prior experiences with treating OUD, the evidence supporting ED-initiated buprenorphine, contextual factors related to ED-initiated buprenorphine, and strategies to facilitate the adoption of this practice.

Interviews and focus groups were audio recorded, transcribed verbatim using a professional transcription service, and uploaded to Nvivo software (version 12).

2.3 Data Analysis: At least two of the three members of the coding and analysis team (MAJ, EJE, KFH) independently reviewed each transcript. Using a codebook previously developed for Project ED Health, the coding team discussed the first 4 transcripts line-by-line after individual review, adding new codes as they emerged from the data.²⁹ An iterative coding process used the constant comparison model to refine the codebook until thematic saturation was reached. An audit trail was maintained. After all transcripts had been coded, ideas that were found to be common across transcripts were identified and sorted into themes. A recurrent cross-sectional approach was used to evaluate for changes over time.³³ Data was triangulated with matrices developed during the Rapid Assessment Process and member checking was conducted with research team members that were not part of the coding team.

2.4 Ethics Statement

The content of this project reflects the authors' own research, and analysis has been carried out in a truthful and complete manner, properly crediting the study co-authors and contributors. All authors have meaningfully contributed to a substantial portion of the work of this project, and have approved of the contents this paper. The research team has worked to intentionally uphold the principals of informed consent, confidentiality and privacy among study participants, ensuring that all participants are anonymous and cannot be identified by demographic information. Finally, this project adheres to the principle of beneficence, as it works to improve access to evidence-based treatment

among individuals with opioid use disorder, a vulnerable population within our healthcare system.

2.5 Summary of Student Contributions

MAJ (student) was responsible for development of methodology, implementation of computer software, formal analysis, data curation, preparation creation, and presentation of published work, writing the original draft, and data visualization. KFH was involved in study conceptualization, development of methodology, validation, formal analysis, investigation, project administration, provision of resources, data curation, writing-original draft, supervision, project administration, and funding acquisition. GD was responsible for study conceptualization, methodology, investigation, writing- review and editing, funding acquisition, and supervision of the project. EJE was responsible for study conceptualization, development of methodology, formal analysis, conducting the investigation process (collection of evidence), provision of resources, writing-review, and editing. DAF was involved in study conceptualization, methodology, investigation, writing-review and editing, and funding acquisition. POC, ED, PO, and SM were involved in methodology, investigation process, data collection writing-review and editing. MC, EC, ML, LR, RR, LW, and EZ were involved in data collection, writing-review and editing. EZ was involved in writing-review and editing.

3. Results

3.1 Participant characteristics: A total of 15 individuals participated in 8 focus groups or interviews (range 1-3 pharmacists; Table A). There was a total of six focus groups and two interviews.

3.2 Themes:

Six themes were identified in accordance with the PAHRIS framework (Table B). Evidence themes included (1) varied levels of comfort and experience among ED pharmacists with ED-initiated buprenorphine that increased over time and (2) a perception that patients with OUD have unique challenges that are relevant to ED care that can be addressed through guidance. Context themes included ED pharmacists' ability to (3) clarify scope of ED care in the context of unique pharmacology, formulations, and regulations of buprenorphine, and that (4) clinical pharmacists streamline local processes necessary for successful program implementation. Facilitation themes included (5) a need for local training to promote practice change and (6) a need to leverage already existing pharmacy resources outside of the ED.

3.2.1 Theme 1: Experience with ED-initiated buprenorphine varied among ED pharmacists and increased over time (Evidence)

Participants described varying levels of baseline comfort with the practice of ED-initiated buprenorphine among clinical pharmacists within their institution. One participant described the practice as being counter-intuitive to many clinical pharmacists, contributing to discomfort with the practice.

“I think the biggest barrier right now is that people don't know that we could do that. It's kind of the opposite of probably what most of the pharmacy staff think that they can do, as far as if they see an order for that. They would question it, and probably try to get it not approved, because they don't think it's allowed.” (Site A/pre-IF/p1)

While some were aware that initiating buprenorphine was the preferred strategy to treat withdrawal and knew where to find specific information about the practice, they still lacked the specific knowledge about how to do so.

“It's more noticeable to people as far as what's available in the literature and lectures and blogs and everything else about we should be starting buprenorphine, but they don't really know how to use it or what to do with it... We see that people are making this conscious effort to try to do something, but they are not particularly knowledgeable about what they're doing.” (Site B/ Pre-IF/p1)

In addition to lack of general knowledge, lack of experience with the practice contributed to feelings of discomfort. This lack of experience, paired with a general lack of adoption of the practice by EDs participating within this study, led pharmacists to take additional efforts to reorient themselves to the specific steps required to carry out the practice. Greater experience was identified as a factor necessary to increase fluidity and comfort with the practice.

“I've had some experience with it but I haven't had a ton of experience with it. It's very, as we've said earlier, sporadically. I feel like over the month I talked about it a couple of times and then I don't really talk about it for a while. Then I have to go back and dig out my resources again and be like, ‘Okay, what do I know about this? Based on this patient's specific factors that I know about, this is what I think we should do.’” (Site B/ Pre-IF/p2)

“I haven't had a lotta experience with seeing somebody who's coming in opioid use disorder and is acutely started on buprenorphine and seeing how that impacts them.” (Site C/Pre-IF/p1)

Some pharmacists described understanding of the overall pharmacology of buprenorphine and other MOUD across all time points. However, they also reported that their unfamiliarity with the literature supporting ED-initiated buprenorphine, contributed to a lack of comfort with the use of buprenorphine in their EDs.

“I think, from the standpoint of knowing how it works, the pharmacology, I’m very comfortable. In terms of understanding the literature that’s out there for using it in the ER and rapid induction or that kind of thing, I’m a little less familiar just because I myself haven’t read all the literature. Pharmacologically, I get it.” (Site C/Pre-IF/p1)

In contrast, others reported that while patients with OUD commonly presented to their ED, because methadone was the primary MOUD used within their community, ED clinical pharmacists felt unfamiliar with the use of buprenorphine in general.

“We do see a lotta people coming in with history of opioid use disorder... I feel like a lotta people don’t really know much about it. That’s one of the reasons that it’s such a new and novel idea here because most people we see are coming in on methadone therapy... or they’re self-medicating, so there’s not really a lot of familiarity with using buprenorphine, at least in this setting.” (Site B/ Pre-IF/p2)

“I’m going to admit... I know it exists and it’s my to-do list of things I need to read and figure out... I can’t say that I know much about starting in the emergency department to facilitate long-term buprenorphine therapy, that I’m not super-familiar with it.” (Site B/ Pre-IF/p1)

Though pharmacists identified the high prevalence of OUD in their EDs, they also cited lack of existing protocols and experience with using buprenorphine in the ED as a barrier to treating OUD when compared to other chronic conditions.

“I liken it to a CHF exacerbation. We probably see opioid withdrawal on the same order as CHF exacerbation, but I know how to handle a CHF exacerbation without having to think about it as much. I don’t feel that level of comfort with withdrawal patients.” (Site B/ Pre-IF/p1)

Over the course of the study period, and as EDs developed and implemented protocols to promote buprenorphine use, clinical pharmacists described increasing comfort with the use of buprenorphine. They also detailed their ability to support the practice both in real time and through quality improvement. One pharmacist described an overall increase in comfort among prescribers once a departmental protocol was established, noting the importance of 24-hour pharmacy support to facilitate this.

“The [buprenorphine administrations] that I’ve looked over, they’ve been fine. They’ve all unfortunately been times where there wasn’t a pharmacist available. However, we just started having pharmacists on overnight last week. That should help with that. I think it’s a pretty order set-driven process, which they can do very independently. I think they’ve all gotten good education. I’m sure there’ll be questions as things come up.” (Site A/IF/p1)

Another pharmacist described the implementation and growth of ED-initiated buprenorphine in their ED as evolving over time, with initial concerns and reservations mitigated by the existence of a clear protocol and a change in culture.

“It’s pretty clear that we are definitely going in the right direction. From my end, I know that we are definitely prescribing more buprenorphine for patients... I think it’s almost like autopilot now for us, whereas, before, it was more of a “Oh my god, we’re really doing this... In the beginning, what I saw was a little bit of... resistance... it was a pain for them. But once everyone got on board and it was just normal for us, it wasn’t a big deal.” (Site D/post-IF/p1)

3.2.2 Theme 2: Patients with OUD have unique challenges relevant to ED care that can be managed with guidance or protocols (Evidence)

In pre-IF focus groups and interviews, clinical pharmacists identified unique challenges for initiating buprenorphine treatment in patients with OUD as barriers to care. These barriers included the absence of protocols to guide patient selection, a lack of existing

infrastructure to support referral to outpatient care, and limited medication access. Some clinical pharmacists described concerns about patient readiness to engage in care.

“I just think from a resource standpoint, just seeing how we are now, I don't know that we have the resource available in the community to take on that patient volume. I also don't know willingness of patients, and I think that's something I'm a little less familiar with. If it's not something they're really ready to do, is it reasonable to offer it or is it not?” (Site B/ Pre-IF/p1)

Additionally, clinical pharmacists reported concerns about patient ability to obtain medication and participate in care following discharge from the ED. They also conveyed concern that patient access to ongoing care following discharge might be limited given the complicated social situations that many patients with OUD face.

“I'm just worried, at night, if somebody came in and they wanted to discharge a patient on buprenorphine*, and [the patient is] uninsured or homeless, then right now we don't have a way to make sure we can help get that.” (Site A/pre-IF/p1) [*Trade name replaced]

“I know there are several health systems and states that are starting to do this and are doing it very successfully. I think my impression and kind of the overarching knowledge that I have of it is that they have a mechanism to get people engaged in care. I'm not convinced that we successfully are going to be able to do that.” (Site B/pre-IF/p1)

Moreover, pharmacists noted that they faced unique challenges when attempting to treat pain in patients with OUD, highlighting the need for additional education on appropriate analgesia. They also stated that staff members' stigma surrounding OUD often prevented patients' concerns with pain from adequately being addressed.

“I think we try to treat pain, but there’s definitely, obviously, some educational opportunities for pharmacists and providers to know about the best way to treat their pain... I think that there are always some comments of well, “they’re a heroin addict, they’re going to be difficult to control their pain. Or they’re on buprenorphine*, so maybe the pharmacist will recommend using a different analgesic’.” (Site A/pre-IF/p1)

Participants also initially reported that because buprenorphine was not commonly perceived as a first line analgesic for patients presenting within participating EDs, as well as the need to engage in specific QI initiatives, the treatment of pain and opioid withdrawal simultaneously was a unique challenge that complicated the practice of ED buprenorphine.

“When patients first come in we have a tendency to be like, ‘let’s give you something for pain up front’, because we have pain scores that we need to meet and that kind of stuff... I would say the number of patients who have withdrawal issues... are here for other medical conditions as well, and so trying to tease out the balance between those two things.” (Site B/pre-IF/P1)

Because of pain management concerns, as well as perceived complexities of prescribing, pharmacists indicated that the lack of ED buprenorphine-related prescribing protocols hindered implementation. Despite the lack of protocols, many desired to participate and support the practice.

“I think it depends on how it’s set up and if everybody has a defined role. I feel like that really impacts flow. Everyone has to know what the purpose is and have a defined process... I feel like, if you have it set up to run smoothly, then it will work.” (Site C/pre-IF/p1)

Moreover, they also conveyed the ways in which further protocolization surrounding which specific buprenorphine formulation to use would lead prescribers to feel more

comfortable with ED buprenorphine, leading to greater ability of clinical pharmacists to promote the practice.

“So they know that, if they don’t have a contraindication and they have a COWS score of X, then they should give this dose so that it becomes a lot easier for the providers” (Site B/pre-IF/p2)

“We don’t have a defined protocol in terms of, would we give methadone versus clonidine or whatever, to manage withdraw symptoms, kind of like a MINDS protocol, like a CIWA. I wouldn’t say that we have anything really defined for opioid use disorder. I think it really is clinician dependent in terms of how they manage.” (Site B/pre-IF/p1)

“The only other question is just clarifying or teasing out the different buprenorphine products since there are so many new products coming out. Just if we were to come up with some guidelines or protocols, making it very clear which one should be used and what they're for.” (Site B/pre-IF/p2)

Participants described the importance of setting up an order driven pathway to clarify questions and support clinical practice, even in the absence of real-time pharmacist support.

3.2.3 Theme 3: Pharmacists have the ability to clarify scope of ED care in the context of unique pharmacology, formulations, and regulations of buprenorphine to ED staff members (Context)

Early on, clinical pharmacists relayed a sense of unease around the process of prescribing buprenorphine in conjunction with other ED clinicians. Despite this, ED pharmacists indicated that they felt uniquely positioned to address these concerns. This was in part due to their constant presence in the ED, which differed from other clinicians.

“An attending may be here four or five times a month. They'll come to us and say, “What have you been doing? How do I do this? I haven't done this before.” ...That's our strength is that we are the consistent people, day in and day out... we'll get the volume in terms of seeing a lot of bup patients.” (Site B/IF/p3)

“Not everybody will be knowledgeable about everything here right away, because there are all these different people putting pieces together, but we probably know. Even though that seems so weird, and we're not even here, we probably do know who each person is that's doing something. If you ask a question, we probably can.” (Site A/IF/p2)

Multiple pharmacists reported clinician uncertainty surrounding how to safely prescribe buprenorphine, and the differences in safety concerns and dosing between buprenorphine and methadone.

“I also think our prescribers have a lotta misinformation about how to use both of the drugs... There's misinformation about how many doses of methadone I can give in a 24-hour period for an acute withdrawal patient and feeling like they're not responding yet, so I need to escalate that dose and trying to ensure that they understand the safety concerns with that versus buprenorphine where you can do a little bit more dose titration in a 24-hour period with a little bit less risk associated.” (Site B/IF/p2)

Moreover, they also reported confusion over different buprenorphine formulations but acknowledged their ability to address such gaps in knowledge.

“Providers get confused, all the time, of like what the difference between suboxone, Subutex, Zubsolv.” (Site B/post-IF/p2)

In addition, pharmacists were keenly aware of impending policy changes, and were often heavily involved in the dissemination of such information. Pharmacists highlighted their role as an on-the-ground real-time resource to ED staff for medication protocols, as well as regulatory and clinical policies.

“If there’s a policy change and a legal change, and if it’s a policy involving a drug, then we’re going to be involved in it... I would say any of our policies that involve drug dosing or use or anything like that, we do get super involved with, especially at a teaching institution, because that’s a large percentage of questions that we get. “What do we do here?”” (Site A/pre-IF/p2)

In some cases, they even worked to obtain documentation that answered questions surrounding the legality of the practice, further clarifying scope of care.

“We actually have a letter on file from the DEA clarifying all of that, so that if there is any pushback, ever, we can say oh, actually, there you go.” (Site A/IF/p1)

3.2.4 Theme 4: Pharmacists help streamline local processes necessary for successful program implementation (Context)

Clinical pharmacists described their role as integral to the adoption of ED-initiated buprenorphine in ED settings. More specifically, they described working to ensure smooth implementation of the practice through deliberate collaboration with ED staff members. Importantly, they acknowledged their role as a trusted resource to ED staff, including to nurses who may be new to or uncomfortable with administering buprenorphine.

“I had to walk a nurse through the guideline and explain why we were doing what we were doing... cause [the physician] wanted to give another dose, which is

clinically appropriate to do, and the nurse is like, “I’m not giving it,” and so I was like, “Okay, well, let’s talk through your concerns. We’ll talk through why this is appropriate.” At the end, she was fine.” (Site B/post-IF/p2)

In many cases, clinical pharmacists played an important role in facilitating direct medication access for patients by completing administrative tasks such as prior authorizations and other paperwork for medication assistance programs.

“The pharmacy medication assistance team initiates the prior authorization. A lot of times, I’ll request them, and I’ll work with the team. We’ll do the prior authorization.” (Site A/IF/p2)

Additionally, pharmacist-led quality improvement (QI) initiatives were important in monitoring frequency of buprenorphine prescriptions and were used to gauge success of program implementation.

“We have a dashboard that we can monitor for lots of different things related to opioid prescribing, and one of them is buprenorphine prescribing... We can narrow it down to our department based on who’s X-waivered, how many prescriptions they’re writing per month, per year—whatever the timeframe we want it to be.” (Site B, Post-IF, p1)

Pharmacists also played an important role in the implementation of naloxone programs. In one ED, pharmacists developed a policy for how to identify high-risk patients in need of naloxone prescriptions and created naloxone-related educational material for patients. Pharmacists were also key drivers of QI initiatives to improve naloxone distribution.

“One of the things that I’m working on right now is somehow getting Epic to trigger an automatic naloxone prescription when any opioid is prescribed. Even if somebody’s being discharged from trauma or something.” (Site A/IF/p2)

3.2.5 Theme 5: Need for local training to promote practice change (Facilitation)

Most pharmacists were highly motivated to engage in the implementation of ED-initiated buprenorphine, but reported a need for additional training early on. More specifically, during early implementation, pharmacists called for training in an outpatient setting to help them gain experience with and clarify their role in buprenorphine initiation.

“From a pharmacy perspective, we're having a little bit of difficulty finding our place in the process. We really want to be intimately involved... but we want to be in that outpatient follow-up setting... We want to see how those practitioners can troubleshoot because we might be getting similar types of questions in the ED. We want that real-life hands-on experience, and we've had difficulty setting that up.” (Site B/IF/p3)

Additionally, they identified a desire to be offered the same training (e.g., DATA 2000 X-waiver training) as prescribers to allow for uniformity in understanding of the practice.

“I think whatever education and training we're giving our provider colleagues, it would be helpful if we had it as well, not only for our learning purposes but also to ensure that they are interpreting what they're learning.” (Site B/Pre-IF/p1)

In addition, participants also cited the multitude of patient presentations as a barrier to implementation, and suggested incorporating potential patient scenarios and pathways into the training process to help promote a better understanding and facilitate adoption of this practice.

“You need to have specific scenarios and educate to them what exactly and how you would handle that scenario. If someone on buprenorphine was hit by a truck, what would you do? Somebody in acute withdrawal who's on buprenorphine, what would you do? Going through all of these scenarios and having a pathway for them to figure out... Because it's confusing and there's so many different

scenarios... They don't necessarily understand the difference... It doesn't intuitively make sense. Just helping them out navigate the process and how to handle someone acutely in an emergency department setting is what we really need." (Site A/Pre-IF/p1)

Over time, the importance of streamlining access to training resources and protocols was broadly recognized as necessary for success. Multiple pharmacists noted the importance of "making it easy".

"It needs to be as easy as possible, I think, for the providers and the nurses just because, if it seems like a lotta work, I think people won't do it. But when you show them that someone else has already developed these resources, you just have to implement and use them and post them for hospital-wide use, I think it's much more easily accepted." (Site D/Post-IF/p1)

3.2.6 Theme 6: Interdepartmental collaboration among pharmacists supported program development (Facilitation)

A need for collaboration with clinical pharmacists from other departments was also common. This was of particular importance when addressing patient presentations and treatment strategies that ED pharmacists had limited experience with, such as during early program implementation.

"I definitely tap my pain and palliative care pharmacist colleague, friends, to say, "Hey, what would you do here? We're not quite familiar with this."" (Site B/Pre-IF/p1)

They also noted that pharmacists within other departments were similarly interested in buprenorphine initiation, and that working with these pharmacists could improve organizational efforts.

“We have pain and palliative care specialists who are actually heading this opioid clinical community, so it is very much in the forefront of their minds... it’s just a matter of getting the disciplines from a medical standpoint all in the same room.” (Site B/Post-IF/p1)

Over time, ED clinical pharmacists described increasing comfort with the use of buprenorphine in the ED, such that they perceived themselves to be a hospital-wide resource on the use of buprenorphine.

“Because we’re the only ones that really see it as much as we do. I think our general sense is that this is a great— it’s a very effective tool, and it’s being implemented.” (Site D/Post-IF/p1)

4. Discussion

To our knowledge, this is the first qualitative study that examines the facilitators and barriers to the adoption of ED-initiated buprenorphine with ED pharmacists in effort to help inform implementation strategies. Key barriers to practice implementation include variance in initial pharmacist experience of provision of buprenorphine that increased over time, perceptions that improved protocols may address specific challenges of implementing these programs, and the absence of clinical pharmacist presence within certain times within the ED. Our findings also highlighted the ability of pharmacists to effectively assist in education and implementation of novel practices based on their unique role in ED settings, and posits opportunities to further facilitate pharmacist involvement in the implementation of ED-initiated buprenorphine through additional pharmacist training and interdepartmental collaboration among pharmacists.

The American College of Emergency Physicians, the American Academy of Emergency Medicine and the American College of Medical Toxicology have both endorsed the administration of buprenorphine within the ED as a bridge to ongoing OUD treatment.^{34,35,36} Additionally, these groups have emphasized the critical role that pharmacists play in multidisciplinary ED care.³⁷ Despite this, our study found that pharmacists initially reported varied levels of comfort with ED-initiated buprenorphine, and cited ED staff perceptions of patient specific factors as barriers to adoption of the practice. This is consistent with previous literature that has similarly reported discomfort with the practice among ED clinicians as a result of limited experience and perceived lack of treatment engagement within patients with OUD following discharge.^{29,38,39} This discomfort may reflect underlying stigma that has dominated the narrative of treating patients with OUD within the healthcare system, and future efforts should focus on implementation of additional department-wide educational opportunities to allow for cultural shifts within the ED to better implement buprenorphine.

Clinical pharmacists also cited lack of pre-existing department-wide protocols to aid in ED-initiated buprenorphine as a barrier to comfort with the practice. This finding is in alignment with prior literature within ED clinicians which has demonstrated the ways in which increased protocols not only helps to increase ease of prescribing, but also signals buy-in of evidence-based practices of department leadership with regards to treatment of individuals with OUD.²⁹ As such, implementation of clear and specific protocols for ED buprenorphine through integrating the Clinical Opiate Withdrawal Scale (COWS) and subsequent algorithm for prescribing guidelines within the electronic medical record

system may encourage practice change by both signaling practice support by key stakeholders and reducing the cognitive load necessary to successfully carry out the practice.

Additionally, the absence of continuous pharmacist presence in the ED was also cited as a barrier to successful practice implementation of ED-initiated buprenorphine. As such, our results further support calls by the American College of Medical Toxicology for 24-hour staffing of dedicated Emergency Department pharmacists to optimize medication administration and improve outcomes within the ED.⁴⁰ This is of particular interest given the current landscape of growing staffing shortages within Emergency Departments, and the ways in which pharmacist presence has the potential to address such gaps in care.³⁷

Our study also demonstrates the ways in which clinical pharmacists can provide educational and regulatory guidance to staff members, and play an important role in the implementation of processes to treat OUD within the ED. These findings underscore and expand the well-established benefit of ED pharmacists in optimizing timely patient care and improving clinical outcomes. For example, in the treatment of acute ischemic stroke, pharmacists can participate in patient care by mixing tissue plasminogen activator (tPA) ahead of time to lead to rapid access when necessary, screen for individual contraindications to tPA among patients, and ensure correct tPA dosing. Because of such contributions, it has been shown that pharmacist presence leads to a reduction in door-to-recombinant tissue plasminogen activator (rtPA) time by twenty minutes.⁴¹

Additionally, clinical pharmacists play an important role in antimicrobial stewardship and treatment of sepsis in the ED through dosing recommendations and recommendations for appropriate additional empiric antibiotics. Their presence has been shown to lead to shorter time periods to antibiotic administration and increased the number of patients that received appropriate antibiotics when presenting with septic shock^{42,43}. With regards to antimicrobial stewardship, their presence reduces time to review of previous laboratory and culture results and reduces ED readmission rates following culture review.⁴⁴⁻⁴⁶

Pharmacists also contribute to processes that promote smooth transitions of care following a patient's ED visit. They contribute to this process by reviewing patients' home meds and assessing patient administration technique prior to discharge, identify contraindicated medications, collaborating with ambulatory pharmacists outside of the ED, and intervening on errors in discharge medication. Pharmacist led intervention has been shown to improve disease state understanding among patients, and in one study demonstrated pharmacist intervention on 10% of discharge prescriptions to prevent medication errors.^{47,48} Their presence also improves outcomes in trauma resuscitations, and has been shown to decrease time to postintubation sedative and analgesic use.⁴⁹

Our findings add to the existing body of knowledge that demonstrates significant contributions by clinical pharmacists in the use of buprenorphine and the prevention and treatment of opioid use disorders.^{26,50,51} For example, within the inpatient setting, multiple pharmacist led opioid interventions led to reduction in opioid prescription at discharge.^{48,52} Pharmacists also can contribute to OUD prevention within an inpatient

setting post-operatively through reviewing discharge plans with collaborating clinicians and providing counseling and education to patients regarding pain management.⁵³ In the outpatient setting, pharmacists in some states serve as consultants at opioid treatment programs to oversee MOUD compounding and dispensation, and work with program leadership to establish pharmacy policy backed by evidence based practice.⁵⁴

We found that pharmacists often initiated QI projects, including those aimed at improving EHR clinical pathways targeting naloxone distribution and buprenorphine prescribing. Pharmacist involvement in naloxone distribution is an effective strategy to expand overdose treatment, as exemplified by the near 100-fold increase in retail pharmacy naloxone prescriptions from 2007 to 2016 that resulted from the passage of naloxone access laws.⁵⁵ Pharmacists led naloxone-based harm-reduction initiatives have served as an important community resource to provide overdose education and increase naloxone uptake among individuals with OUD.⁵⁶

Moreover, pharmacy distribution of non-prescription needles through syringe service programs have been associated with a decrease in syringe sharing behavior.^{57,58}

Additionally, a recent open-label feasibility trial in which participants' buprenorphine care was transferred from their office-based buprenorphine treatment (OBBT) physician to a community pharmacist demonstrated the potential for collaborative practice agreements to expand the role of clinical pharmacists in ongoing buprenorphine treatment. As evidenced by their involvement in QI projects expanding access to harm reduction measures, pharmacists are well positioned to be local champions for ED-

initiated buprenorphine, and have a nuanced understanding of pharmacology, policies and protocols, and regulatory knowledge that is helpful in this process.

Finally, our study puts forth suggestions for future strategies that can be adopted to better engage ED pharmacists in the implementation of ED-initiated buprenorphine. Additional training of ED based clinical pharmacists in an outpatient setting could help clarify the role of pharmacists in this process, as well as help to troubleshoot common roadblocks to buprenorphine initiation that they face in the ED. For example, pharmacists could gain additional experience and training in office-based opioid treatment (OBOT) and opioid treatment programs (OTP) that prescribe buprenorphine. Pharmacists also called for parallel training with other clinicians to allow for them to provide better staff education, specifically related to DATA 2000 waiver training. Increased access to clinical training for pharmacists is in alignment with a 2022 American Pharmacists' Association policy calling for "pharmacists' independent prescriptive authority of medications indicated for opioid use disorders (MOUDs)... to expand patient access to treatment".⁵⁹ Moreover, entering into collaborative practice agreements with and removing DEA-mandated prescribing limitations imposed on community pharmacists could further expand the clinical pharmacist's role in transitions of care to outpatient buprenorphine treatment following discharge from the ED.^{26,60} Finally, collaboration with pharmacists from other departments, such as palliative care, psychiatry, and pain management, could provide additional education opportunities to facilitate implementation of ED-initiated buprenorphine.

All in all, this study's findings suggest that pharmacists are well positioned to play a role in facilitating the adoption of ED-initiated buprenorphine. Specific strategies to achieve this goal include facilitating clinical experience with buprenorphine for pharmacists who support ED staff through training in outpatient settings, exposure to shared protocols from other institutions and interdepartmental collaboration amongst pharmacists. Future efforts to implement such initiatives have the potential to optimize ED care and improve the treatment of patients with OUD.

4.1 Limitations

As is the case with qualitative research, findings from this study may not be generalizable to all pharmacists or EDs. Our focus group sizes were limited by the number of clinical pharmacists that staff the ED at each institution, along with their availability. Because of limited availability among participants, and because participation was anonymous, there were times at which there was a disparate number of participants at one study site across time. For example, at study site B, there were 3 participants during the pre- and post- IF period, but only 2 participants during the IF period. Although our study size is small, prior work supports a high likelihood of reaching thematic saturation within 3 to 6 focus groups among a homogenous group of participants using a semi-structured interview guide.⁶¹ Further, our findings were found to be consistent with other data sources collected as part of the Rapid Assessment Process that was conducted during the parent study. An additional limitation is that focus group facilitators and interviewers were physicians, which could potentially increase the presence of social desirability bias

among participants, although this was mitigated by interviewers being from outside institutions.

Since the study was conducted in an urban, academic setting, findings may not be generalizable to community and rural EDs, and in particular those without real-time ED pharmacist support. Moreover, applicability of study findings may vary by ED characteristics such as patient volume and hours of ED clinical pharmacy services. Finally, bias may arise as a result of two group facilitators (KFH, EJE) also participating in the coding process. However, the lead study author (MJ), who also participated in the coding, did not facilitate any focus groups. To enhance transparency of our study and findings, the Standards for Reporting Qualitative Research (SQSR) was used.⁶²

Dissemination

Findings from this project were presented as an oral presentation at the 2022 Society for Academic Emergency Medicine Annual Conference in March of 2022 in New Orleans, Louisiana. They were also presented at the 2022 Association for Multidisciplinary Education and Research in Substance use and Addiction (AMERSA) conference in November of 2022 in Boston, Massachusetts. The manuscript was submitted for publication in the Journal of Substance Abuse Treatment in September of 2022 and is currently under review.

Table A. Designations of interviewees by site and date of interview

Cite	Date	IF Timepoint	Participant Number	Role	Designation
Site A	10/19/18	Pre-IF	1	Pharmacist	Site A/PreIF/p1
			2	Pharmacist	Site A/PreIF/p2
	03/01/19	IF	1	Pharmacist	Site A/IF/p1

			2	Pharmacist	Site A/IF/p2
Site B	04/21/18	Pre-IF	1	Pharmacist	Site B/Pre-IF/p1
			2	Pharmacist	Site B/Pre-IF/p2
			3	Pharmacist	Site B/Pre-IF/p3
	09/19/18	IF	1	Pharmacist	Site B/IF/p1
			2	Pharmacist	Site B/IF/p2
			3	Pharmacist	Site B/IF/p3
	10/01/19	Post-IF	1	Pharmacist	Site B/Post-IF/p1
			2	Pharmacist	Site B/Post-IF/p1
	Site C	07/26/18	Pre-IF	1	Pharmacist
01/20		Post-IF	1	Social Worker	
			2	Pharmacist	Site C/Post-IF/p1
Site D	07/24/20	Post-IF	1	Pharmacist	Site D/Post-IF/p1

Table B. Themes organized according to three domains outlined in PAHRIS framework

Domain	Theme
Evidence: research, clinical experience, local data	1. Experience with ED-initiated buprenorphine varied among ED pharmacists and increased over time
	2. Patients with OUD have unique challenges that require guidance to optimize ED care

Context: culture, leadership, evaluation	3. Pharmacists can clarify scope of ED care in the context of unique pharmacology, formulations, and regulations of buprenorphine to ED staff members
	4. Pharmacists help streamline local processes necessary for successful program implementation
Facilitation: purpose, role, skills, attributes	5. Need for local training to promote practice change
	6. Interdepartmental collaboration among pharmacists supported program development

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