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PRN OPINION PAPER

Mobilizing pharmacists to address the opioid crisis: A joint opinion of the ambulatory care and adult medicine practice and research networks of the American College of Clinical Pharmacy

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Abstract

The opioid crisis represents one of the largest failures of our current health care system as it continues to claim lives at an unprecedented rate and has caused a devastating range of preventable morbidity. Although the availability of highly potent synthetic opioids has amplified the urgency of the crisis for patients and communities, this problem has evolved over several decades. Pharmacists are in a position to offer many potential solutions due to their widespread accessibility, extensive drug knowledge, and integration into various health care settings. This opinion paper challenges the status quo by calling on all pharmacists to embrace evidence-based opioid stewardship and harm reduction practices, contribute to the medical management of

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opioid use disorder, and address the misconceptions and prejudices that serve as barriers to effective, compassionate patient care. Regardless of practice setting or available resources, pharmacists can take deliberate and impactful steps to address the opioid crisis. Some pharmacists may be positioned to implement innovative and far-reaching pharmacist-led clinical services, while others may simply begin with careful consideration of the language they use when speaking to and about patients with substance use disorders. To optimize patient outcomes, the ineffective laws, regulations, and policies that negatively impact pain and addiction care must be addressed so that evidence-based solutions can be widely disseminated. Pharmacists must aggressively advocate for the removal of barriers preventing high-level clinical practice or policies that perpetuate patient harm and abandonment. Finally, there must be support for continued research on pain and opioid use disorder treatments and services, as well as the impacts of harm reduction practices and pharmacist-led clinical services, so that resources can be allocated effectively.

KEYWORDS

harm reduction, opioid epidemic, opioid-related disorders, pharmacists, social stigma

1 | INTRODUCTION

Clinical Scenario 1: A woman with chronic low back pain and a 15-year history of daily opioid use is referred to the clinical pharmacist to develop an opioid tapering plan. The provider wants to reduce the patient's daily morphine milligram equivalents (MME) to below 90 mg as quickly as possible—"then we will see if we can stop it completely because opioids don't even help with back pain…plus the director flagged my average MMEs as being too high this quarter." The provider requests that the clinical pharmacist meet with the patient to complete her care plan for the day, including urine drug screening, prescription monitoring program evaluation, and naloxone education.

A series of five hypothetical clinical scenarios likely to be encountered by a pharmacist are offered with each major section. See the Clinical Scenario Considerations for guidance on each scenario.

1.1 | Shifting landscape of opioid-related harm

Situations resembling Clinical Scenario 1 are becoming increasingly common and shine a spotlight on how far the pendulum has swung in opioid prescribing and pain management.[1] The 1990s to 2000s were a time of increased pain awareness, when organizations such as The Joint Commission and American Pain Society championed the effort to make pain "visible," so that it could be managed effectively.[2] Pain was labeled as the "fifth vital sign," and opioids became a quick solution to short- and long-term pain needs. At the time, opioids for therapeutic indications were thought to rarely lead to addiction. A substantial increase in opioid prescribing ensued, peaking in 2010.[3,4] The incidence of opioid-related fatal overdoses[5] and the prevalence of opioid use disorder (OUD) also increased steadily during this time frame.[6] By 2010, drug overdose was the leading cause of injury death in the United States and opioids were involved in a majority of these fatalities.[7] The staggering rate of fatal opioid overdoses has led to a range of responses from regulatory bodies.

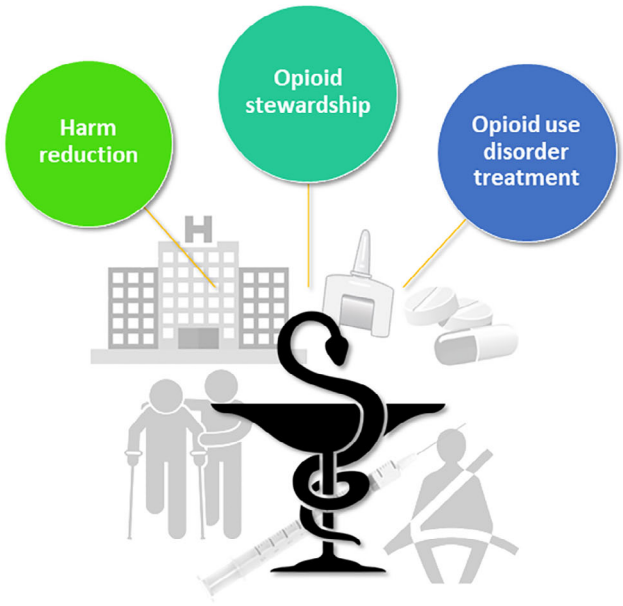
The release of the Centers for Disease Control and Prevention (CDC)'s *Guideline for Prescribing Opioids for Chronic Pain* in 2016 represented a landmark moment in the effort to address rising rates of opioid-related harm in the United States.[8] The guideline contains 12 broad recommendations aimed at enhancing opioid prescribing safety among primary care providers. Importantly, these recommendations were offered with caveats for patient-specific implementation and an implementation guide was later issued[9] to assist with the integration of guideline principles into practice. Before and after issuance of this guideline, many states adopted laws and regulations to restrict opioid prescribing and dispensing.[10-12] These and other restrictions have resulted in many unintended consequences, such as increased use of nonregulated and nonprescription opioids, untreated OUD, suboptimal chronic pain management, poor quality of life, involuntary opioid tapering and discontinuation, and suicide.[13-16] Concerns relating to misapplication of the CDC guideline prompted its authors to publish a commentary reiterating that these guidelines should not be strictly implemented at the population level.[17]

The CDC estimates there were 46 802 fatal overdoses involving opioids in 2018.[18] Until recently, the rate of unintentional fatal opioid overdoses had been increasing, though currently only the rate of fatal overdose from synthetic opioids (eg, illegally manufactured fentanyl) continues to climb.[5,18,19] Clinicians are now being advised to consider screening all adults for illegal drug use,[20] limit opioid prescribing for only chronic, severe and/or unrelenting pain syndromes, co-prescribe naloxone, prioritize life-saving medications for OUD (MOUD), and refer patients to services that enhance their long-term recovery.[8] This is a dramatic and rapid change for health care providers and their patients. Pharmacists must rise to the challenge at hand, lending their drug and disease management expertise to health care teams across the spectrum of care to prevent avoidable deaths and other morbidity, while continuing to improve care for patients with acute and chronic pain.

1.2 | Pharmacist's role in advancing evidence-based solutions

The optimal approach for achieving positive patient outcomes is through a comprehensive model of opioid stewardship and increased access to harm reduction resources and evidence-based MOUD. This approach must also include compassionate and comprehensive treatment of pain. The Joint Commission has employed pain assessment and management standards, including specific elements of performance surrounding safe opioid prescribing. While opioid stewardship is not required by The Joint Commission, it is an inferred recommendation from several regulatory agencies. Opioid stewardship can be universally described as "coordinated interventions designed to improve, monitor, and evaluate the use of opioids in order to support and protect human health"[21]; however, a standardized definition currently is lacking. While several governmental and regulatory agencies, including The Joint Commission, do not delineate the specific role of the pharmacist, most advocate that pharmacists play an integral role on opioid stewardship teams. Pharmacists ensure safe and effective opioid therapy, implement harm reduction strategies, reduce stigma associated with opioid use and OUD, facilitate medication-based addiction treatment, optimize pain management, perform patient and provider education, and advocate for broader pharmacist privileges to co-manage OUD and pain management pharmacotherapy.[21,22] See Figure 1 for examples of pharmacist activities.

It is crucial that opioid stewardship programs do not focus solely on supply reduction strategies, as harm reduction strategies are more effective at preventing opioid-related mortality and morbidity.[23] Harm reduction strategies prioritize the minimization of negative consequences associated with a risky behavior, such as illegal drug use, rather than seeking to force abstinence from that behavior.[24] These interventions often target patients at highest risk for substance-related harm, such as those with current or recent illegal substance use and intravenous drug use. It is vitally important that pharmacists recognize the unintended consequences of supply reduction strategies applied in



Harm reduction

- Providing sterile injection education and distribution of injection equipment
- Educating on overdose reversal and naloxone distribution
- Providing fentanyl testing strips and educating on safe use of unknown illegal opioids
- Screening for HCV and HIV, administering immunizations, and recommending pre-exposure prophylaxis
- Educating on safe opioid storage and disposal
- Facilitating wound care and triage

Opioid stewardship

- Developing and implementing evidence-based opioid treatment plans
- Developing opioid order sets, prescribing protocols, and guidelines
- Initiating and modifying non-pharmacologic and non-opioid therapies
- Conducting prospective and retrospective case reviews
- Developing and implementing opioid taper plans
- Evaluating high-risk drug/disease combinations (e.g. opioid-benzodiazepine)
- Developing and implementing controlled substance agreements
- Interpreting qualitative and quantitative toxicology test results
- Monitoring for opioid misuse by patients and healthcare professionals

Opioid use disorder treatment

- Initiating and modifying pharmacotherapy (e.g. buprenorphine and naltrexone)
- Monitoring and follow-up (e.g. observed daily dosing, toxicology results)
- Facilitating adjunct services (e.g. mental health, HCV and HIV therapy) and wrap-around patient resources (e.g. transportation, housing, employment)
- Addressing stigma and negative attitudes towards treatment and PWUD
- Advocating for patients and the expanded role of the pharmacist in treatment

FIGURE 1 Pharmacist involvement in harm reduction, opioid stewardship, and opioid use disorder treatment. This figure shows activities and services in which pharmacists may be involved and is not intended to be all inclusive. Many activities are subject to state and federal law, which pharmacists must know and adhere to. HCV, hepatitis C virus; HIV, human immunodeficiency virus; PWUD, people who use drugs. All images are licensed under Creative Commons BY 2.0

isolation and become outspoken advocates for harm reduction strategies.

Pharmacists must also work to enhance identification of patients with OUD and facilitate access to evidence-based MOUD. Although OUD is largely managed by addiction specialists and primary care physicians (PCP), the available supply of professionals in these disciplines is insufficient. Using data from the Substance Abuse and Mental Health Services Administration (SAMHSA), 96% of states had insufficient capacity to meet treatment demands.[25] Pharmacists play a major role in meeting these demands by actively treating OUD and engaging patients with OUD to improve outcomes.[26] Additionally, pharmacists can help eliminate treatment barriers including insurance coverage, restrictive state and federal policies, and treatment stigma, which is prevalent among patients, their family members, and health care workers.

The following opinion paper is intended to provide insight into the current opioid crisis and offer pragmatic steps for pharmacists to become involved in opioid stewardship, harm reduction, and the management of OUD. Furthermore, this paper will discuss the numerous barriers to care and identify opportunities for continued pharmacist advocacy and training. Although this paper represents the opinion of the Ambulatory Care and Adult Medicine Practice and Research Networks of the American College of Clinical Pharmacy (ACCP), it is not considered an official ACCP commentary, guideline, or statement of position or policy.

2 | HARM REDUCTION

> Clinical Scenario 2: The clinical pharmacist enters the examination room and can immediately see the patient is anxious about the impending discussion. "It's a pleasure to meet you. Your doctor asked me to speak with you today about some of the risks associated with your opioid pain medication." She replies defensively, "I've been taking the same one for 15 years. I'm not a junkie. I need this medicine." The clinical pharmacist adjusts his approach. "I understand that your medicine is important to you, and I don't want to take it away or change your dose today. Is it ok if we talk about a new medicine that can help keep you safe while you continue taking opioids? It's called naloxone."

2.1 | Prioritizing harm reduction

According to the Harm Reduction Coalition, "Harm reduction is a set of practical strategies and ideas aimed at reducing negative consequences associated with drug use. Harm Reduction is also a movement for social justice built on a belief in, and respect for, the rights of people who use drugs."[24] Available evidence indicates that harm reduction interventions should be the first priority for pharmacists seeking to address the current crisis of opioid-related morbidity and mortality in the United States.[23]

2.2 | Overdose education and naloxone distribution

Naloxone is a life-saving medication when administered for the reversal of acute opioid overdose. The medication antagonizes opioids present in the central nervous system by strongly binding opioid receptors and temporarily displacing receptor-bound opioids for 1-2 hours.[27] Currently, naloxone is available in several formulations appropriate for administration by a layperson, such as intranasal or intramuscular routes.[28] Two recently approved products using each of these routes of administration have been shown to have advantages regarding ease of use and may thus be preferable when increased cost is not a barrier.[29-32] When used, naloxone can restore normal respiration and consciousness in the overdose victim.[11] Improving access to naloxone has become a national priority endorsed by the Surgeon General, and every state has enacted at least one naloxone access law (NAL) to achieve this goal.[33,34] Community-based models for take-home naloxone through harm reduction coalitions, substance use disorder (SUD) treatment programs, and syringe service programs (SSP), also known as syringe exchange programs, have been in place for decades in the United States with impressive results.[12,35] However, SSPs are illegal in 15 states, and 93% of counties deemed high risk for an outbreak of human immunodeficiency virus (HIV) or hepatitis C virus (HCV) have no SSP. They are particularly rare in rural areas, highlighting the importance of rural pharmacists in enhancing access to naloxone and other harm reduction supplies.[36]

The 2016 *Guideline for Prescribing Opioids for Chronic Pain* recommends that clinicians offer patients naloxone when risk factors for opioid overdose are present (eg, history of overdose, SUD, use of high-dose opioid analgesics, or concurrent benzodiazepine).[8] Co-prescribing naloxone to patients with chronic pain receiving opioids in primary care settings was associated with a 47% reduction in opioid-related emergency department visits in one observational trial, and multiple studies have demonstrated that patients are receptive to overdose education and there is a high willingness to prescribe naloxone in primary care settings.[34,37,38] Despite this evidence of efficacy, multiple studies have demonstrated that the majority of patients at high risk for opioid-related overdose have not been dispensed naloxone.[39,40] Multiple contributing factors to suboptimal naloxone co-prescribing have been identified amongst prescribers, including a lack of knowledge regarding how to prescribe it, to whom it should be prescribed, and how to educate patients about its use.[38] Legislative mandates which require naloxone co-prescribing for certain high-risk patient populations have been associated with a substantial increase in naloxone dispensing, indicating legislative or regulatory action may be necessary to achieve and sustain substantial increases.[41,42] The

Food and Drug Administration (FDA) has recommended that all MOUD and opioid manufacturers include naloxone in their prescribing information to be discussed with patients.[43]

State-level enactment of a NAL is associated with increased naloxone dispensing and reductions in fatal overdose.[44-46] The specific elements of state NALs vary with inconsistent inclusion of legal protections for overdose victims and witnesses who seek emergency medical services, as well as rare inclusion of naloxone co-prescribing mandates. However, NALs tend to include three core components: (a) expanded authority for pharmacists to distribute naloxone; (b) allowance for third-party prescribing to individuals who may witness an overdose; and (c) broad liability protection for health care professionals and overdose responders. State approaches to expand pharmacists' authority to distribute naloxone may have an impact on population-level outcomes as well. A recent analysis found that granting pharmacists "direct authority" to distribute naloxone (ie, dispensing naloxone without a prescription) is associated with a 27% to 34% reduction in overdose mortality while granting "indirect authority" (eg, statewide protocol or standing order) was not associated with a significant reduction.[47] However, the true impact of increased pharmacist autonomy through direct authority NALs remains unclear. Mounting evidence indicates that pharmacists are not taking advantage of authority under state NALs and do not possess sufficient knowledge to effectively identify high-risk patients and provide overdose education.[48-51] Similar findings are seen in other countries such as Australia, where naloxone is available behind-the-counter.[52] Academic detailing is one viable solution for improving pharmacist knowledge about naloxone and the likelihood that naloxone will be stocked and dispensed in community pharmacies.[53-56] Larger, collaborative initiatives such as the ONE Rx program in North Dakota offer a promising framework for expanding community pharmacist screening for opioid misuse and potential for overdose, but is still limited by low "reach" (number of patients screened) and "implementation" (number of pharmacies completing at least five screenings) when evaluated under the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) model.[57]

A rapidly growing body of research explores the role of pharmacists in naloxone distribution and education across numerous practice settings.[34,55-60] Pharmacist involvement in these programs has ranged from program development and provider training to patient identification and education. Pharmacists in all health care settings should establish automatic protocols to identify patients at risk for overdose and proactively offer naloxone with comprehensive education to patients as well as their friends, family, and caregivers, who may be responsible for administering naloxone during an emergency.

2.3 | Syringe access and injection safety

Persons who inject drugs (PWID) are at risk for serious infections including HIV, hepatitis B virus (HBV), HCV, and severe bacterial infections such as endocarditis. Hospitalizations for infections in PWID in the United States increased dramatically from 301 707 (2002) to 520 275 (2012), with related inpatient charges increasing to $15 billion.[61] Access to sterile syringes has the potential to curb these increasing rates of preventable illness and expense. Pharmacists play a key role in maintaining and expanding access to sterile syringes, providing education about safe injection technique, and assuring safe syringe disposal.[62]

SSP are typically community-based prevention programs providing access to sterile syringes, drug preparation equipment, and safe disposal at no cost to PWID.[63,64] The range of services provided through SSPs may be limited to only sterile syringe access or include a variety of additional harm reduction and OUD services. These programs have long been recognized as a means for decreasing transmission of HIV, HBV, and HCV.[65,66] Following full implementation of a structured SSP in New York, investigators reported a 29% decrease in HCV prevalence (P = .034) and a 40% decrease in HIV and HCV co-infection prevalence in PWID (P < .01).[66] Following introduction of the first SSP pilot in Florida in 2016, there was a 49% decrease in syringes found in public areas.[67] Importantly, these data can stimulate swift changes to state syringe laws, such as the passage of Florida's Infectious Disease Elimination Act in 2019 following these pilot data. Also, SSPs are increasingly recognized as an opportunity to engage patients with SUDs who otherwise may not be ready to participate in treatment discussions.[63,65] The US Surgeon General supports SSPs as part of a set of comprehensive morbidity and mortality-reducing interventions for the opioid crisis.[68] In addition to syringe access, many PWID are unaware of their eligibility for pre-exposure prophylaxis, which has also been shown to significantly reduce HIV transmission.[69,70] Community pharmacies offer an ideal venue for syringe exchange and other services for PWID, as they already offer syringes and wound care products and can offer related screening, treatment, and educational services by pharmacists and interns.[71] In states such as Minnesota, where syringe access legislation promotes pharmacy dispensing of sterile injection equipment, over 60% of community pharmacists surveyed were comfortable dispensing syringes from their pharmacy.[51] Unfortunately, in many states, paraphernalia and syringe access laws, as well as stigmatizing business policies, severely limit pharmacists from engaging PWID to the fullest extent possible.

2.4 | Medication storage, security, and disposal

Providing counseling on (a) storage of opioids in a locked container; (b) keeping opioids in their original package; (c) keeping opioids out of children's reach; (d) not sharing medication with others; and (e) safely disposing of unused pills are all key pharmacist roles. Appropriate disposal of unused prescription opioids is crucial for reducing harms associated with both unintentional ingestion and suicide. Improving patient knowledge about proper disposal can mitigate unauthorized access to medications and reduce unintentional ingestions among children.[72] The primary source for prescription opioids for nonmedical purposes is family and friends (Figure 2).[73,74]

Pharmacist-led initiatives to improve patient knowledge about opioid disposal can make a significant difference. Providing patients information on drug disposal programs at local pharmacies along with a small incentive, such as a coupon, was associated with a 22%

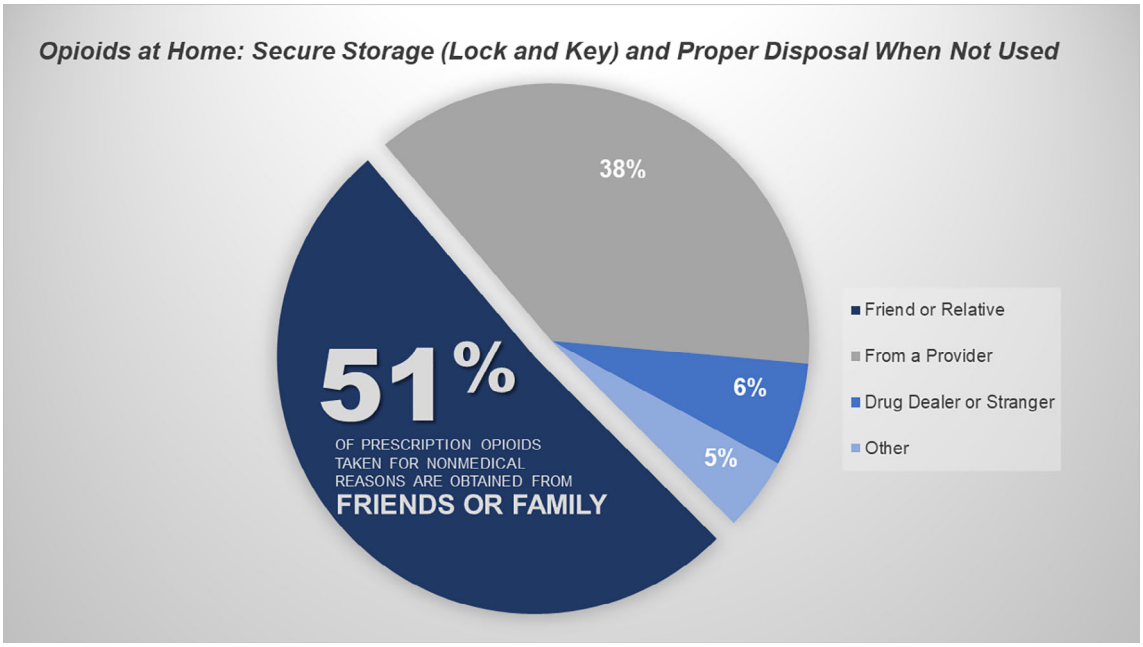


FIGURE 2 Sources of prescription pain relievers for nonmedical use. Data are from the Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration 2018 National Survey on Drug Use and Health.[73] Percentages are approximate as values were rounded to the nearest whole number

increase in the proportion of patients disposing their unused opioids following dental procedures.[75] Drug disposal education is becoming more prevalent, but there are opportunities for improvement. In a recent analysis, approximately 61% of survey participants stated they received counseling on medication disposal from a health care professional within the past year which increased the likelihood for medication disposal by 67%.[76] However, most of this education was not being done by pharmacists, who were identified as the source for this counseling only 21% of the time.[76] Highly regulated and advertised medication drop boxes and drug takeback days are also effective, though low-cost and easily implemented educational interventions (eg, informational brochures) seem to have a significant impact on disposal rates as well.[77-79]

Guidelines developed by the US Office of National Drug Control Policy, and Environmental Protection Agency for the disposal of household pharmaceuticals include (in order of preference): (a) use a drug take-back event or drop box; (b) dispose in household trash after mixing the medication with an unpalatable substance (eg, free manufacturer provided charcoal pouches, commercially available drug disposal kits, cat litter, or coffee grounds) and placing the mixture in a sealed container; and (c) flush the unwanted medicine down the toilet if the drug label specifically instructs you to do so (40 C.F.R. Sect. 266.505).[80] Medication mail-back envelopes, an additional option that may be helpful for homebound and hospice patients, have demonstrated a nearly 4-fold increase in the odds of opioid disposal when available.[81] Patients who would prefer to bring their medications to pharmacies for disposal may do so after the pharmacy registers with the US Drug Enforcement Administration (DEA) as a "collector," allowing them to receive controlled substances for destruction. Current regulations do not require a particular destruction method, so long as the medication is rendered "nonretrievable" in compliance with applicable federal, state, and local laws.[81]

3 | OPIOID STEWARDSHIP

Clinical Scenario 3: Members of a clinic's interdisciplinary Opioid Task Force are discussing a patient receiving chronic opioid therapy who has recently tested positive for tetrahydrocannabinol on a urine drug screen. The patient's PCP starts the conversation, "…although their urine was clean last month, it was dirty this month. She's been stable, but this breaks our contract." Due to the infraction, the decision is made to discontinue the patient's opioid. The Chair of the Task Force asks clinical pharmacy to put together a taper plan that can be implemented before their next fill, while making sure to "check the prescription drug monitoring program (PDMP) to make sure we're the only ones prescribing."

3.1 | Opioid stewardship: An evolving practice

The term, "opioid stewardship" is used to describe efforts to prioritize appropriate opioid use while reducing opioid misuse in a variety of

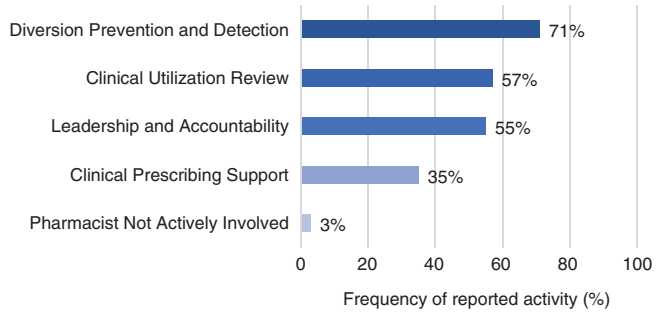


FIGURE 3 Hospital pharmacist activities and involvement in opioid stewardship programs.[82] Percentages have been rounded to the nearest whole number

health care settings. The prevalence of opioid stewardship programs has been increasing steadily, with over 40% of hospitals reporting an active opioid stewardship program in 2018.[82] Although these programs have different approaches to stewardship, the most common activities include (in rank order): clinician education and guideline development; routine PDMP inquiries; prioritization of nonpharmacologic and nonopioid pain management strategies; and opioid diversion detection. Pharmacists are becoming increasingly accountable for opioid-related quality measures.[83] Figure 3 describes the most common pharmacist activities in opioid stewardship programs. Here we propose a more robust definition, supported by national leaders and accrediting bodies.[21,49,84,85] Opioid stewardship encompasses an interprofessional, multidisciplinary, and holistic approach to addressing opioid prescribing through monitoring and education, while optimizing multimodal pain management and harm reduction practices, preventing and managing OUD, and using clinical decision support tools and quality metrics to drive decision-making. Pharmacists are a vital part of opioid stewardship efforts and have a tremendous opportunity to place people before policy. As such, we assert that pharmacists should assume a leadership role within the stewardship team.

3.2 | Opioid management: Prescribing, regulations, and harm reduction

Despite the availability of numerous clinical practice guidelines, guidance on individualized opioid prescribing for acute and chronic pain management is highly variable and often based on expert opinion due to the limited evidence available.[86] Therefore, it is crucial that pharmacists carefully review individual opioid regimens. Specifically, pharmacists should be involved in assessing initial appropriateness of opioid therapy in collaboration with an interprofessional team; designing and implementing opioid prescribing protocols, electronic health record prompts, and order sets to leverage safe prescribing; and monitoring opioid therapy using applicable health information technology and clinical decision support tools. Even small changes, such as setting low quantity defaults on prescription opioid order sets (eg, 10 tablet default), can affect prescribing practices across an entire institution.[87] Furthermore, in order to benchmark opioid stewardship program success and ensure the service aligns with the Quadruple Aim,[88] pharmacists should actively participate in the development and monitoring of opioid-related quality and performance measures.[83]

Evidence is insufficient for the routine use of opioids for chronic noncancer pain (CNCP), though there is good-quality evidence of a dose-dependent risk for serious harm.[89] When opioids are started early for pain management and at high doses, the likelihood for opioid persistence increases significantly,[90,91] which in turn increases the risk for numerous negative health outcomes, including: addiction, fractures, sexual dysfunction, and various gastrointestinal, cardiovascular, central nervous, respiratory, and endocrine system disturbances and events.[89,92] It should be noted that for some patients, the risk vs benefit is acceptable, while for others it is not. Having a pharmacist involved early during treatment is especially important to identify alternative pain management strategies. Nonpharmacologic and nonopioid therapies should be exhausted prior to initiating opioid therapy, with the goal of improving function, reducing pain, and minimizing the harms associated with opioid use. These opioid-sparing therapies should be continued, or sometimes intensified, concurrently with opioid therapy. Lastly, when opioids are warranted for CNCP, clinicians must carefully consider dose, formulation, and duration based on a careful assessment of functionality, pain, and risk mitigation for which standardized assessment tools are available.[8]

In the last few years, numerous stakeholders and policymakers have enacted rules and regulations that limit the duration of opioid prescriptions for acute pain or initial prescriptions, in order to curb opioid-related harms.[93] High-dose opioid regimens have also been scrutinized, sometimes leading to involuntary tapers. An opioid taper may be indicated for some, such as when the risks outweigh benefits, clinically meaningful improvements in pain are not achieved, or opioid-induced hyperalgesia is suspected.[8,17] Furthermore, guidelines exist to help clinicians through important taper considerations, such as how to individualize taper rates and strategies for managing opioid withdrawal.[94] However, the effect of mandatory opioid tapering policies on patient stability and well-being is concerning.[95] Only very low-quality evidence supports tapering long-term opioid therapy[95,96] and the risk for negative health outcomes (fatal overdose and suicide) associated with opioid cessation increases rapidly in patients who have received continuous opioid therapy for long periods of time.[16] Pharmacists can help identify appropriate candidates for tapers, implement taper plans that minimize withdrawal symptoms, and monitor patients for negative health outcomes (eg, suicidal ideation) after a taper has begun. In many circumstances, alternate harm reduction strategies such as co-prescribing naloxone and managing high-risk opioid combinations (eg, benzodiazepines) may be more appropriate to consider. It should be noted that high-risk opioid combinations cannot always be avoided, especially when patients are stabilized or dependent on those concomitant high-risk medications. Nonetheless, pharmacists must support individualized opioid treatment plans, lending their extensive drug knowledge to other clinicians and patients navigating complex drug-drug and drug-disease interactions and instances of misapplied guidance from clinical practice guidelines.

Patient-clinician relationships based on mutual respect and understanding are paramount for effectively managing any chronic disease, pain included. In some instances, it may be necessary to formalize treatment goals and expectations through controlled substance agreements (CSA).

3.3 | Controlled substance agreements

Although frequently utilized in practice, very little high-quality evidence supports the use of CSAs as a means to improve patient care or prevent side effects and diversion.[97] Guidance on CSAs suggests they should be written to: improve adherence, obtain informed consent, outline prescribing polices, and mitigate the provider's legal risk.[98] However, in a survey of PCPs, the majority viewed CSAs as a means to reduce professional liability and reduce contact with patients.[99] This is concerning, as patient safety and wellbeing should be at the center of these agreements. Well-written CSAs should focus on patient safety, while incorporating principles of shared decision-making, ensuring appropriate readability, and be applied consistently. Many example CSAs are available (eg, National Institute on Drug Abuse Sample Patient Agreement Form, available from: https://www.drugabuse.gov/), which serve as a starting point that can be adapted to ensure the above criteria are met for each unique patient care setting.

3.4 | "Abuse-deterrent" formulations

Abuse-deterrent opioid formulations (ADF) are also viewed as promising advancements by many health care researchers and policy leaders. An ADF opioid is formulated to deter known or common routes of misuse—primarily crushing for insufflation or dissolving for injection—through a number of different strategies (eg, physical/chemical barriers or opioid agonist/antagonist combinations).[100] Although the recommendations in the FDA's guidance for industry are considered nonbinding, companies are required to conduct postmarketing evaluations of all FDA-approved ADFs with abuse-deterrent labeling claims.

The majority of FDA-approved ADF opioids are relatively new to the market, so there is limited postmarketing data available to judge their impact. The most promising results of ADF opioids appear to occur initially after the introduction of the new formulation. Studies show decreases in the prevalence of opioid misuse with ADFs vs previous formulations of the drug.[101] To this end, manufacturers have achieved their stated goal of deterring misuse. However, this does not paint the whole picture. The introduction of crush-resistant formulations, rendering tablets impossible to insufflate, is associated with increasingly dangerous injection practices to circumvent the technology. For example, the ADF technology used in Opana® Extended Release (ER) makes the oxymorphone poorly soluble and requires more water to fully dissolve, which increases injection burden to 2-4 injections per injection episode.[64] Subsequently, HIV and HCV outbreaks and injection-related thrombotic microangiopathy correlate with ADF technology.[64] In conclusion, ADFs represent a significant cost to the health care system and evidence supporting their use is insufficient.[23,102-105] In fact, some models predict that ADFs will increase opioid-related mortality over the next decade.[23] Therefore, continued research is needed to clarify the role of ADFs for preventing opioid misuse and pharmacists should stay current with knowledge about the intended and unintended consequences of ADFs.

3.5 | Prescription drug monitoring programs

The PDMP is another increasingly popular tool among policymakers. All 50 states have some form of PDMP, which is used by clinicians to guide decision-making and by law enforcement to track various patterns of opioid use and prescribing. Use of PDMPs is associated with reduced opioid prescribing,[106] reduced rates of high-risk opioid use, and increased screening for SUD.[107] Furthermore, several variables tracked by PDMPs (eg, high opioid doses and multiple pharmacies/providers) correlate with the presence of an OUD diagnosis.[108] Subsequently, there are many ongoing efforts to increase PDMP utilization and efficiency through state mandates and software integration. However, clinicians are still learning about the full impact of this powerful surveillance tool on the current opioid crisis. The effects of PDMPs on fatal and nonfatal overdose rates have been mixed—some studies showing an increase, while others showing a decrease—and the aggregated evidence supporting their use is considered low-strength.[109] Furthermore, the effect of PDMPs on overdose rates seems to vary based on specific program features (eg, nonscheduled drug monitoring) and state regulations. Historically, interventions like PDMPs that reduce prescription opioid access have led to increased use of illegal opioids, as these interventions abruptly drive patients away from prescription opioids. Taking this and other factors into context, this shift toward illegal opioids caused by PDMPs may actually precipitate a net increase in fatal opioid overdoses over the next decade.[23] When PDMP surveillance is warranted, use should be applied uniformly to improve treatment safety and efficacy. When discrepancies arise, they should prompt clarifying conversations between the patient and provider, rather than abrupt opioid cessation and patient abandonment. Pharmacists must also fully consider the ethical dilemma posed by requests for PDMP data from law enforcement pursuing criminal investigations. These requests should always be accompanied by a court order or directed at the PDMPs themselves (vs individual pharmacists).[110]

3.6 | Universal screening

Although most patients who use opioids will not develop an OUD, a small number will develop a pattern of problematic opioid use. The US Preventive Services Task Force draft guidance recommends universal screening of adults 18 years old and older for SUDs based on evidence of a moderate net benefit, but stipulates that implementation

occur when accurate diagnosis and treatment can be provided in response to a positive screening.[111] Screening, Brief Intervention and Referral to Treatment (SBIRT) is a useful framework for identifying, reducing, and preventing substance misuse.[112,113] Theoretically, universal screening for SUD would identify patients in need of help sooner and lead to an appropriate linkage to care. However, attempts to integrate SUD screening into different health care settings has have been met with mixed results. Some studies evaluating screening and intervention tools have shown a benefit,[114-116] which may persist months beyond the brief intervention,[114] while other studies have failed to show a significant benefit.[117,118] Therefore, screening and intervention tools should be developed specific to the needs and resources available to each practice setting. Screening can be completed quickly by pharmacists and other clinical staff and validated tools, such as SBIRT, should be integrated into health records and pharmacy dispensing software for ease of tracking and monitoring.[119,120] Furthermore, although there is a temptation for pharmacists to use PDMP reports for OUD screening, combining these data with validated screening tools is more beneficial for identifying patients at risk for OUD.[61,121] Support from administration and department leaders, and sustainable payment models[122] are needed for increased SUD screening, particularly for integrating these services into community pharmacy settings. Furthermore, when OUD screening tools are utilized, their impact on health outcomes is necessary to ensure consistency and appropriate transitions through care.

4 | OUD TREATMENT

Clinical Scenario 4: Several providers at an outpatient clinic have been asking about "treatment options for opioid addiction." The director of medical services has responded by asking clinical pharmacy to help develop a new addiction service in collaboration with the family medicine providers and staff. Extended-release intramuscular naltrexone is chosen for the protocol due to its perceived effectiveness and low administrative burden, "…so long as patients detox in the hospital." Furthermore, it is the only FDA-approved medication a pharmacist can prescribe through a collaborative practice agreement in their state. Six months into the pilot program, the pharmacy team becomes frustrated by the high no-show rate and wishes to add buprenorphine to the protocol. However, only one provider has an X-waiver and the staff are concerned this addition will increase the weekly appointment load and "headaches with insurance and pharmacies." The pharmacy team is now tasked with exploring buprenorphine prescribing models that integrate pharmacists while minimizing administrative burden.

4.1 | Treatment access and an overreliance on abstinence-based treatment

Treatment for OUD includes psychosocial/behavioral interventions and MOUD (Table 1). Despite decades of data helping clinicians recategorize OUD as a chronic, relapse-remitting, neurologic disease, the number receiving treatment remains low. The most recent statistics indicate only 34.5% of persons with OUD have received any type of treatment within the past year.[123] Furthermore, abstinence-based treatment still dominates the landscape.

Treatment plans that exclusively rely on an opioid taper followed by abstinence are generally considered inferior to MOUD and increase patient harm.[124,125] However, this very approach remains the most prevalent type of treatment offered for OUD in the United States. As of 2017, among the 13 585 facilities offering treatment for OUD, only 9.5% offered methadone, 29% offered buprenorphine, and 24% offered extended-release naltrexone (XR-NTX).[126] Of the facilities offering MOUD, rarely did they offer all three MOUDs, further limiting options for patients.[127,128] OUD treatment should be individualized based on demonstrated treatment efficacy/safety, severity of illness, risk of relapse, patient preference, treatment history, access/availability, cost/coverage, and family/support. However, many federal and state regulations, as well as wholesaler, practice, and payer-specific policies, have led to a lack of access to evidence-based MOUD and an over-reliance on programs offering less effective abstinence-based programs.[25,129] Even for those seemingly lucky few who obtain MOUD, the benefits may not be fully realized, as these medications are often discontinued prematurely for a variety of reasons.

4.2 | Medication-first treatment approach

Use of opioid agonists (methadone or buprenorphine) to treat OUD is associated with more than a 50% reduced risk for fatal overdose.[127,130] Therapies this effective are rare, yet MOUD remains underutilized due to lack of treatment access and capacity for patients.[25,127] Patients face an unacceptable 4- to 7-year lag between OUD onset and initial receipt of treatment in the United States.[127] The issue, at least in part, is created by stringent US regulations on medication-based treatment. In countries such as France, providers are empowered to prescribe MOUD such as buprenorphine with few excess restrictions, which has led to far higher treatment rates.[131] This highlights a critical need to revise rules and regulations that impede access to MOUD in the United States.

To combat low utilization of MOUD in Missouri, a medication-first treatment approach has been developed.[132] The tenets of this approach are that patients should receive MOUD quickly; MOUD should be continued as maintenance therapy without arbitrary tapering or discontinuation, unless the patient's condition has worsened; and individualized psychosocial services should be offered, but refusal of these services should not affect medication access. Data 1 year

TABLE 1 Medications for opioid use disorder (MOUD)[195-197]

	Opioid agonist		Opioid antagonist
	Methadone (MTD)	**Buprenorphine (BUP)**	**Naltrexone (NTX)**
Opioid receptor activity	Full Mu Agonist	Partial Mu and Nociceptin Agonist, Kappa and Delta Antagonist	Mu > > Kappa and Delta Antagonist
Formulations approved for OUD or relapse prevention (generics as indicated)	Oral liquid and tablet (generic)	Sublingual and buccal tablets and film with and without naloxone (generic), long-acting subcutaneous injection, subdermal implant	Oral tablet (generic), long-acting intramuscular injection
Controlled Substance	Yes (C-II)	Yes (C-III)	No
General considerations	Federal regulations limit methadone for an OUD indication to outpatient treatment programs certified by SAMHSA CSAT	Naloxone co-formulated products are generally preferred for OUD	High treatment attrition seen with XR-NTX in clinical trials (relative to opioid agonist therapy)
	Allowable take-home quantity varies, but gradually increases over years of treatment	Providers must receive SAMHSA CSAT Waiver and receive a DEA X-number to prescribe for OUD indication	Oral NTX monotherapy is not recommended for OUD maintenance
	High risk for life-threatening respiratory depression, regardless of use with other CNS depressants	Low risk for life-threatening respiratory depression, unless used with other CNS depressants such as benzodiazepines	
	Variable kinetics		
Considerations when starting therapy	Slow, incremental dose titrations	Slow, incremental dose titrations	7–10 day opioid abstinence required
	EKG monitoring for a QTc baseline and regular monitoring during treatment is recommended	Clear and objective opioid withdrawal must be present[a]	Abstinence often confirmed with urine toxicology report and a naloxone or naltrexone "challenge"
	Conservative initial doses are recommended for those with concomitant CNS depressants, respiratory disorders, or age > 60 years old	Home-induction appropriate for most	REMS certification required for parenteral formulations
		Collaboration between inpatient and outpatient services is essential	
Started in Emergency Department?[b]	Rarely	Yes	Rarely
Pharmacist allowed to prescribe through collaborative practice agreements?	No	Sometimes[c]	Yes
Considerations when stopping or changing therapy	Long half-life prolongs tapers and response to dose adjustments	Long half-life prolongs tapers and response to dose adjustments	Oral NTX is sometimes used between XR-NTX injections or to bridge transitions
	Sub-therapeutic MTD doses (eg, 30-40 mg/day) recommended when converting to BUP		

Abbreviations: BUP, buprenorphine; CNS, central nervous system; DEA, Drug Enforcement Administration; ECG, electrocardiogram; ED, emergency departments; MTD, methadone; NTX, naltrexone; QTc, Q-T interval corrected; REMS, risk evaluation and mitigation strategy; SAMHSA CSAT, Substance Abuse and Mental Health Services Center for Substance Abuse Treatment.

[a]Preferably, patients should be experiencing at least moderate withdrawal based on an objective withdrawal scoring tool (eg, clinical opioid withdrawal scale). Buprenorphine can precipitate withdrawal rapidly if started too soon. Micro-dosing buprenorphine induction regimens do exist and are considered exceptions to this rule but have not been evaluated in rigorous clinical trial settings.

[b]Methadone may be administered for 72-hours (not prescribed) for opioid withdrawal management in EDs under the "72-hour rule" (21 C.F.R. Sect. 1306.07(b)).[194] Buprenorphine may be administered for 72-hours for opioid withdrawal management in EDs under the "72-hour rule" (21 C.F.R. Sect. 1306.07(b)), but can also be prescribed for addiction by X-waivered providers. Due to the required opioid abstinence period for naltrexone, a patient starting naltrexone in the ED would need to arrive having already been abstinent from opioids for more than 7-10 days or undergo rapid or ultrarapid opioid detoxification under anesthesia.

[c]Pharmacists in eight states are "mid-level providers" (21 C.F.R. Sect. 1300.01(b28)) and are authorized to prescribe CII-V substances via collaborative practice agreements, but other state/federal regulations may conflict with state-granted privileges.[172]

postimplementation showed significantly improved rates of MOUD-based treatment, reductions in median wait time for MOUD, improved treatment retention, and reduced treatment episode costs when compared with a pre-implementation baseline.[132] It should be noted that all patients included in this analysis were uninsured and all of the 14 participating treatment agencies received State Targeted Response funds through SAMHSA. However, there are many other models for integrating medication-based therapy into different care settings, several of which include pharmacists.[133,134] As treatment models evolve, there must be a greater emphasis on continued treatment with MOUD (ie, "maintenance"), vs focusing exclusively on treatment initiation.

Continued use of MOUD is associated with improved patient outcomes and lower health care costs.[129,135,136] Nearly 20 years ago, it was found that adults with heroin use disorder who received buprenorphine 16 mg/day maintenance therapy had a 75% treatment retention after 12 months (vs 0% for those who received placebo after detox), despite both groups receiving psychosocial therapy.[137] Urine toxicology screens were also negative for illegal substances in 75% of the samples acquired, and addiction severity index scores were significantly lower compared with baseline for the buprenorphine maintenance arm. Similar results have been reproduced[130,138] and can be extrapolated to special populations including youth patients with OUD[139] and patients recently released from incarceration.[140] The effect of continued methadone on health outcomes are comparable with buprenorphine, and both are consistently more efficacious and less costly than abstinence-based therapy.[129,136-138] By contrast, XR-NTX appears to be less efficacious than sublingual buprenorphine within intention-to-treat comparisons,[141] and less cost-effective from health care sector and societal perspectives.[142] Long-acting formulations of buprenorphine have not been compared with XR-NTX, though clinical trials are planned (eg, NCT04219540). In summary, the benefits of continued MOUD outweigh the risks, although side-effects, cost/coverage, and patient choice may interrupt or limit treatment duration and success.

Although evidence clearly supports medication-based treatment, pharmacists' engagement has been limited. Considering the complexity of initiating, adjusting, and maintaining MOUD, the need for pharmacist involvement is compelling. Pharmacists have already played, and continue to play, an integral role in widespread MOUD access in other countries.[131] Involvement of community pharmacists in the United States would have a profound impact on treatment access, given that over 90% of the US population live within 5 minutes of a community pharmacy.[143] Furthermore, the evidence supports pharmacists as having positive attitudes toward MOUD.[71,144] With additional training, community pharmacists could be a powerful advocate for persons with OUD and offer an accessible starting point for recovery. Pharmacists unable to commit to the evaluation and management of OUD can still work with patients receiving MOUD to optimize therapy through monitoring and education. It is especially important for that increased oversight to include medication adherence. Recent estimates of MOUD persistence after 1 year was only 21% in a Pennsylvania Medicaid population.[145] It is likely that at least part of the high MOUD discontinuation rate is associated with modifiable barriers, such as cost/coverage, which pharmacists are well positioned to identify and resolve.

4.3 | Barriers to treatment initiation and sustainable treatment solutions

Treatment initiation occurs in a variety of settings and at different points in a patient's OUD recovery (Table 1). Methadone for OUD is available only through opioid treatment programs certified by the SAMHSA Center for Substance Abuse Treatment in the United States. Unfortunately, opioid treatment programs are not readily accessible for many; nearly 90% of counties have an insufficient number of opioid treatment programs, which has changed minimally over time.[146] However, even with an adequate number of opioid treatment programs, there are still many barriers to successful methadone maintenance, such as supervised daily dosing and maintenance associated with the mandatory services opioid treatment programs are required to provide.[143] Community pharmacists can provide many of these same services directly to patients.[71,131] Buprenorphine is also prescribed outside of opioid treatment programs by a growing number of X-waivered providers (eg, "qualifying physician and other practitioners" including: MD, DO, PA, NPs). Providers eligible for a DEA X-waiver has expanded through several landmark Acts (eg, Drug Addiction Treatment Act, Comprehensive Addiction and Recovery Act, and Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities Act), though recent legislative efforts seek to eliminate the training and registration step entirely (ie, The Mainstreaming Addiction Treatment Act).[147]

Buprenorphine prescribing by X-waivered providers through office-based opioid treatment models represents the largest opportunity to expand OUD treatment access using MOUD. The cornerstone of office-based opioid treatment is providers offering buprenorphine through their current clinical practice to increase availability of OUD treatment to patients who need it.[148] However, even with more treatment facilities offering buprenorphine (14% in 2011 to 29% in 2017),[126] nearly half of the 45 000 approved X-waivered practitioners who are able to prescribe buprenorphine are not actively prescribing.[149] Additionally, existing payment models have not incentivized long-term recovery, as OUD services lack the necessary alignment and integrated economic structures.[122]

Innovative and sustainable outpatient treatment models, such as the hub and spoke model, have assisted with widespread service implementation in Vermont. In this model, opioid treatment programs serve as "hubs" for patients who require more specialized care and oversight, but once patients are stable, they are referred out to a network of "spokes," composed of primary care providers offering office-based opioid treatment.[150,151] Spokes are responsible for monitoring adherence to treatment, coordinating access to recovery support, providing counseling, contingency management, and case management services. This type of collaborative approach to OUD is associated with positive patient perceptions about treatment[152] and can help

generate more X-waivered providers as well as increase training opportunities for all types of health care providers in SUD. Community pharmacies could serve as either hubs or spokes, by referring patients to specialized, intensive, and comprehensive addiction care services after induction, or closely monitoring and adjusting maintenance OUD therapy.[71,131,153]

Although the majority of OUD treatment occurs in outpatient settings,[126] initiation of MOUD in the emergency department (ED) and inpatient settings has demonstrated beneficial outcomes including increased patient engagement and 30-day treatment retention and reduced illegal opioid use.[154-157] Patients who have presented to the ED with a nonfatal overdose are at especially high risk for a subsequent fatal overdose,[125] making OUD treatment all the more necessary. Specialized inpatient consult teams are one viable way to introduce new OUD services to an organization and have demonstrated improvements in OUD treatment access during hospitalization.[156] Also, state Medicaid expansion is associated with lower rates of uninsured hospital encounters for opioid-related events[81] and increased access to OUD and mental health treatment.[158] States that have not expanded Medicaid may see similar improvements with Medicaid expansion due to the scope of services that can be offered during and after opioid-related hospitalizations.

Treatment access and engagement remain challenges when starting therapy. A few of the most substantial barriers include stigma, inadequate reimbursement, lack of institutional support, a lack of expertise, and an inadequate number of X-waivered providers.[159] These barriers must be addressed by medical and regulatory agencies.

4.4 | Changing culture and prescribing barriers

Historically, stigma is the most significant barrier to treatment for OUD. Stigma is often rooted in misperceptions about the underlying pathophysiology of SUDs. Continued use of opioids may be viewed as a moral weakness or willful choice rather than a chronic brain disease heavily influenced by genetic predisposition.[143,160] The first steps toward implementing new OUD services must address underlying misconceptions about OUD and alleviate concerns held by staff, without being dismissive. Resources are available to help organizations gauge staff readiness, pursue cultural changes, and plan MOUD service implementation.[22] With adequate resources and staff buy-in, new services can thrive. Unfortunately, federal regulations stifle that growth by requiring X-waiver training and placing arbitrary caps on treatment capacity. Revising regulations to foster increased treatment access will require unified advocacy. Alongside this issue, we must further understand why some providers do not prescribe to capacity, or even at all once X-waivered, as this can also curtail program efforts.[148]

In 2016, the median monthly patient census for over 3000 buprenorphine prescribing physicians was only 13 patients, which is well below capacity.[161] Interestingly, a survey of physicians not prescribing to capacity cited a lack of adequate psychosocial support for patients as the most significant barrier to prescribing MOUD.[148,162] Although behavioral counseling should be offered to patients with OUD, data supporting increased treatment success with the addition of behavioral support is lacking.[163,164] Concerns about recurrent opioid use and MOUD diversion are also frequently reported provider concerns.[165] A return of disease symptoms, including return to use, or "relapse," is an inherent part of managing any chronic disease and should not be conflated with treatment failure. In fact, relapse rates are lower for SUDs compared with many other chronic diseases.[166] Diversion concerns are also misplaced, as nonprescribed buprenorphine use overwhelmingly occurs to help patients manage their own (or other's) opioid cravings and withdrawal.[167,168] In other words, diverted MOUD is most often used for the same reasons as prescribed MOUD, and increased use of diverted buprenorphine is a signal of the limitations within our current treatment system.

Medication cost/coverage is another major barrier to MOUD, which pharmacists can readily address. Buprenorphine/naloxone coformulated products only recently became generic and XR-NTX remains an expensive brand name medication. Fortunately, recent guidance from SAMHSA has led to the removal of prior authorization requirements for buprenorphine-containing medications on Medicare Part D plans, although coverage of these same medications on state Medicaid plans varies widely.[10,169] In states that expanded Medicaid, a significant increase in buprenorphine/naloxone prescribing was seen as compared with states that did not expand Medicaid.[170] However, less costly alternatives such as buprenorphine monotherapy may be reasonable to consider for patients with limited resources.State and federal restrictions limit pharmacists' ability to initiate, modify, and sometimes even dispense opioid agonists for OUD.[171] Only eight states permit pharmacists to prescribe controlled substances through collaborative practice agreements.[172] Amending state laws in the remaining 42 states is a good starting point for pharmacist advocacy. However, even when progressive state-granted privileges are in place, pharmacists are still unable to become X-waivered due to federal restrictions or are limited to prescribing only certain formulations for MOUD (eg, only oral formulations of buprenorphine can be pharmacist-initiated and modified in California per CA H.S.C. Sect. 11 215).[173] Unclear regulations also contribute to pharmacist hesitancy. Only recently, the California Board of Pharmacy adopted an official policy stating that pharmacists can in fact initiate and modify MOUD such as buprenorphine.[174] Whether intended or not, current state and federal regulations affecting pharmacist-led OUD management favor XR-NTX prescribing over other more effective forms of MOUD like buprenorphine. Therefore, pharmacists must advocate for regulatory changes that enable initiation and modification of all effective forms of MOUD. Removing restrictions on methadone by eliminating the opioid treatment program requirement or allowing opioid treatment programs to adapt to our current needs (eg, mobile opioid treatment programs)[175] are other logical next steps to improving treatment access. However, allowing methadone to be dispensed for OUD in community pharmacies, a practice that has been ongoing in other countries for decades,[71] may be the most impactful next step.[176] While limitations are addressed, pharmacists can still play a key role in supporting recovery from OUD by working collaboratively

with patients, payers, and clinicians to identify and minimize side-effects, improve adherence, and quickly resolve prescribing and dispensing delays, which risk significant consequences.

5 | STIGMA, ADVOCACY, AND TRAINING

Clinical Scenario 5: A community pharmacist wants to become more involved in harm reduction practices, as their city has been hit hard by opioid-related overdose fatalities. The pharmacy's policy on syringe sale has changed over the years and currently the pharmacist can only sell syringes to patients with a prescription for insulin. The store manager is also concerned about employee safety if syringe sales are increased. Furthermore, although the whole pharmacy received training on overdose reversal using naloxone, there's still confusion about the new state law allowing pharmacists to dispense under a standing order. The pharmacist in charge has said that, "until we know the insurance companies aren't going to claw their money back, we have to run it cash only." Discouraged by leadership's response, the pharmacist hopes to first reshape the pharmacy's culture around SUDs and harm reduction.

5.1 | Stigma: A barrier to care

While there are many definitions that exist, one of the earliest definitions of stigma is the perception of someone as less desirable, reducing that individual from "a whole and usual person to a tainted, discounted one."[177] Contemporary definitions further classify stigma as perceived stigma, self-stigma, enacted stigma, and structural stigma—all of which originate from a variety of individual and external factors that may be systematic and unintentional.[178] Put differently, stigma, as it relates to OUD, is complex, multifaceted, and pervasive.

Stigma remains one of the most common impediments to starting and continuing MOUD. The misconception of SUDs as a moral weakness or willful choice rather than a chronic disease has created disparities in public perceptions about SUD vs other chronic conditions such as mental illness.[160,179,180] Specifically, respondents were more likely to prefer social distance, permit discrimination, deny employment, and deny housing for persons with SUD over those with mental illness. Consequently, individuals with OUD are met with challenges such as a limited number of treatment centers, denied employment/housing, and barriers to MOUD by health insurers or during incarceration.[160,181] Even among persons in recovery, the use of MOUD is often perceived as a lack of willpower or "crutch" rather than a step toward recovery.[160] In fact, certain Narcotics Anonymous meetings limit participation for members utilizing MOUD, only referring to those who are entirely abstinent to any opioid (including MOUD) as "clean."[182] Although recovery is a common goal, the use of stigmatizing language and practices discourages use of MOUD, and reinforces the misconception that abstinence-based therapy is preferred.

5.2 | Language impacts patient outcomes

Stigmatizing language is a threat to optimizing the care of patients with SUDs. Unfortunately, a recent analysis of public media indicates the use of stigmatizing language may be increasing.[183] Traditional terminology associated with SUDs focused on the potential moral failings of a person in place of the science of this chronic brain disease.[184] Words such as "addict,", "drug habit," "abuser," "dirty/clean drug screen" promote the notion that those with OUD can simply stop "abusing" substances, and are thereby "dirty" when continuing to doing so, which does not align with our neurobiological understanding of OUD. The stigma promoted through negative language builds barriers to care. Nearly 15% of adult patients in 2018 who identified as needing, but not receiving SUD treatment, did not seek out treatment due to concerns that treatment would lead to their neighbors and community forming negative opinions about them.[73] Additionally, language associated with SUDs has a significant impact on implicit and explicit bias of health care clinicians. Terms like "addict" and "substance abuser," among others, elicit negative bias in health professionals[185] and diminish treatment outcomes.[186] Public awareness and educational campaigns along with professional development strategies seek to combat this stigma.[187] See Table 2 for examples of stigmatizing and preferred terms.

5.3 | Pharmacist advocacy and training

As part of the Oath of a Pharmacist, we vow to "embrace and advocate [for] changes that improve patient care."[188] The opportunities to advocate for opioid harm reduction practices and access to treatment

TABLE 2 Stigmatizing and supportive terminology related to substance use disorder[185,186]

Stigmatizing terms to avoid	Supportive terminology to utilize
Substance abuse, substance dependence, drug habit	Substance misuse, substance use disorder
Addict, drug abuser, junkie	Person who uses drugs, person with a substance use disorder
Clean	Remission, recovery
Clean/dirty toxicology screen	Negative/positive toxicology screen
Relapse	Return of symptoms, continued use
Opioid replacement/ substitution	Medication, pharmacotherapy, medication-based treatment
High-risk group	High-risk behavior
Opioid overdose	Breathing emergency

for patients with SUD are abundant at local, state, and federal levels. Expanding naloxone access through NALs is one example where advocacy may result in substantive improvements in patient outcomes.[47] However, there must also be sufficient pharmacist buy-in, training, and resources, otherwise progress will stagnate despite progressive state privileges.[48] Providing education on harm reduction, opioid stewardship, and OUD early in student training,[189] and supplemental knowledge throughout a pharmacists' career, is essential for building individual knowledge and confidence in these areas.

Doctor of Pharmacy programs have reacted to the opioid crisis in different ways. Some have developed specialized activities centered on overdose response training, but there is no single approach. Collectively, programs are offering nearly 500 different opioid-related activities, categorized as being either education- (65%), service- (23%), research- (22%), practice- (8%), or advocacy-based (4%) activities.[190] However, curricular revisions often take a considerable amount of time and convincing to create change. Postgraduate training programs (eg, residency and fellowship) can react more expediently. Program preceptors and directors should strive to offer direct patient care opportunities in pain and SUD treatment within general postgraduate year one (PGY1) residencies, given the increasing prevalence of hospitalizations for opioid-related complications, as well as ambulatory care postgraduate year two (PGY2) residences, recognizing the crucial role of primary care clinicians in addressing these issues Furthermore, available PGY2 specialty programs in pain and palliative care and psychiatric pharmacy must be expanded. Per the American Society of Health-System Pharmacists Online Residency Directory (2019/2020), there are only 25 accredited pain and palliative care PGY2 programs and 73 accredited psychiatric PGY2 programs nationally.[192] Expanding opportunities for PGY2 training will not only increase pharmacist specialization in the areas of OUD and pain management, but will also provide momentum toward recognizing pain and palliative care, or perhaps addiction medicine, as a pharmacy specialty by the Board of Pharmacy Specialties. Board certification is the gold standard for pharmacists and an excellent way for pharmacists to increase scope of practice and state privileges.[191] Lastly, as with previous areas of practice innovation, payment for cognitive services is required to provoke the systemic change necessary to support pharmacist implementation of effective OUD-related interventions. Changes in Medicare eligibility and coverage through the SUPPORT act (eg, opioid treatment program eligibility for Medicare enrollment and bundled payments for OUD services, including telehealth-based services)[193] are notable improvements, but investment in primary care SUD services is still lacking. The reality is that office-based opioid treatments providing comprehensive medication-based care require additional personnel (eg, case managers, behavioral health consultants, and peer specialists), have increased time spent on visits and care coordination, and new regulatory considerations that serve to disincentivize practices from offering evidence-based care. Therefore, innovative payment models are necessary to support evidence-based and comprehensive care.[122]

6 | CONCLUSION

Current evidence supports a multifaceted and collaborative approach to the opioid crisis. Pharmacists can augment ongoing opioid stewardship, harm reduction, and OUD treatment efforts across the spectrum of care. Efforts to heal damages caused by prescription opioids are warranted but addressing only this aspect of the crisis is shortsighted. There must also be efforts to reduce the harms associated with continued opioid use, both medical and nonmedical, as well as evidence-based and accessible treatment for OUD. In fact, the very language we use to describe our patients and their illnesses can impact quality of life and treatment outcomes. Policies that limit clinicians' ability to practice to the extent of their education and training, impede patient access to care, or potentiate the harms associated with opioid use must be revised to reflect current evidence and needs. Lastly, sustainable funding for training, research, and clinical services must be available to identify and provide the safest and most effective pain and SUD treatment modalities, strategies to reduce harm associated with opioid use, and solutions to ongoing barriers to treatment.

Clinical Scenario Considerations:

For all of the clinical scenarios, a multifaceted, patient-centered solution is required; no single therapeutic approach or policy is sufficient. Furthermore, a collaborative interprofessional approach is ideal to maximize patient benefit. While the ideal response to each scenario may vary in practice, the following suggestions are offered by the authors:

Scenario 1. In this scenario, a pharmacist is consulted to assist a provider in managing a patient's chronic pain. Although notably interprofessional, the request demonstrates a non-patient-centered approach to pain management, likely driven by fear and stigma. It is clear that there are system pressures to de-prescribe opioids. Pharmacists must advocate for patients in these situations, ensuring effective therapies are continued when benefits outweigh harms, and that both the patient and provider have agreed upon realistic and attainable pain goals. There are positives to highlight as well. Specifically, the request for naloxone education demonstrates the adoption of harm reduction principles shown to reduce the incidence of fatal overdose. The pharmacist should involve the patient's friends and family in the conversation about naloxone, as they may be responsible for administering naloxone during an emergency.

Scenario 2. Pharmacists educate patients on naloxone every day, but our approach to these challenging conversations is important. In this scenario, the pharmacist senses the patient's defensiveness and immediately employs a motivational interviewing technique that acknowledges and alleviates the patient's concerns. The focus of this

conversation is shifted away from the patient and is placed on the inherent risks of continued opioid therapy. Instead of giving up on the interaction, the pharmacist emphasizes medication safety by prioritizing a harm reduction intervention proven to reduce emergency department visits and overdose mortality rates to a greater extent than opioid dose reduction.

Scenario 3. In this scenario, the members are discussing how to proceed after a controlled substance agreement (CSA) infraction. Similar to Scenario 1, we see a non-patient-centered approach to pain management. In addition to use of stigmatizing language (eg, "dirty" vs "positive"), the committee has failed to fully understand the patient's reason for cannabis use and has hastily pursued a life-changing decision to taper the patient's opioid therapy. The pharmacist in this case should recognize harms associated with abrupt opioid tapers, advocate for more information regarding the patient's use of cannabis, pain etiology, and response to opioid therapy, and ensure the patient understands their CSA. The patient's responses could aid the team in identifying additional care needs or lead to the conclusion that concurrent cannabis use is acceptable.

Scenario 4. This scenario depicts struggles encountered by a new pharmacist-led opioid use disorder (OUD) service within a family medicine practice. Unfortunately, there are considerable barriers to prescribing opioid-agonist therapies (eg, buprenorphine) in primary care, especially for pharmacists working under collaborative practice agreements, which reduce medications for opioid use disorder (MOUD) options for patients. Pharmacists must resist the temptation to manage OUD with opioid antagonists exclusively and instead advocate for state and federal regulations and reimbursement models that support all forms of MOUD in primary care. In the meantime, the clinic could partner with opioid treatment programs (ie, hub-and-spoke model) or other health care agencies to facilitate, sustain, and expand access to opioid agonist therapy.

Scenario 5. The final scenario describes a pharmacist in the community advancing harm reduction practices at their pharmacy. However, the pharmacist is met with barriers including restrictive syringe and naloxone policies and misconceptions and prejudice toward people who use drugs. Fortunately, store policies can be revised and unclear rules and regulations can be clarified. Changing culture is often more challenging and time-consuming. It will be important for the pharmacist to address staff concerns, as well as educate and consider initial compromise. After gaining momentum, it will then be important to galvanize members around specific outreach and advocacy initiatives, disseminate successes and failures, and connect with other harm reduction agencies in the community.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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