THE OUTBREAK AND SEQUELAE OF THE INCREASE IN OPIOID USE IN THE UNITED STATES, CANADA AND BEYOND

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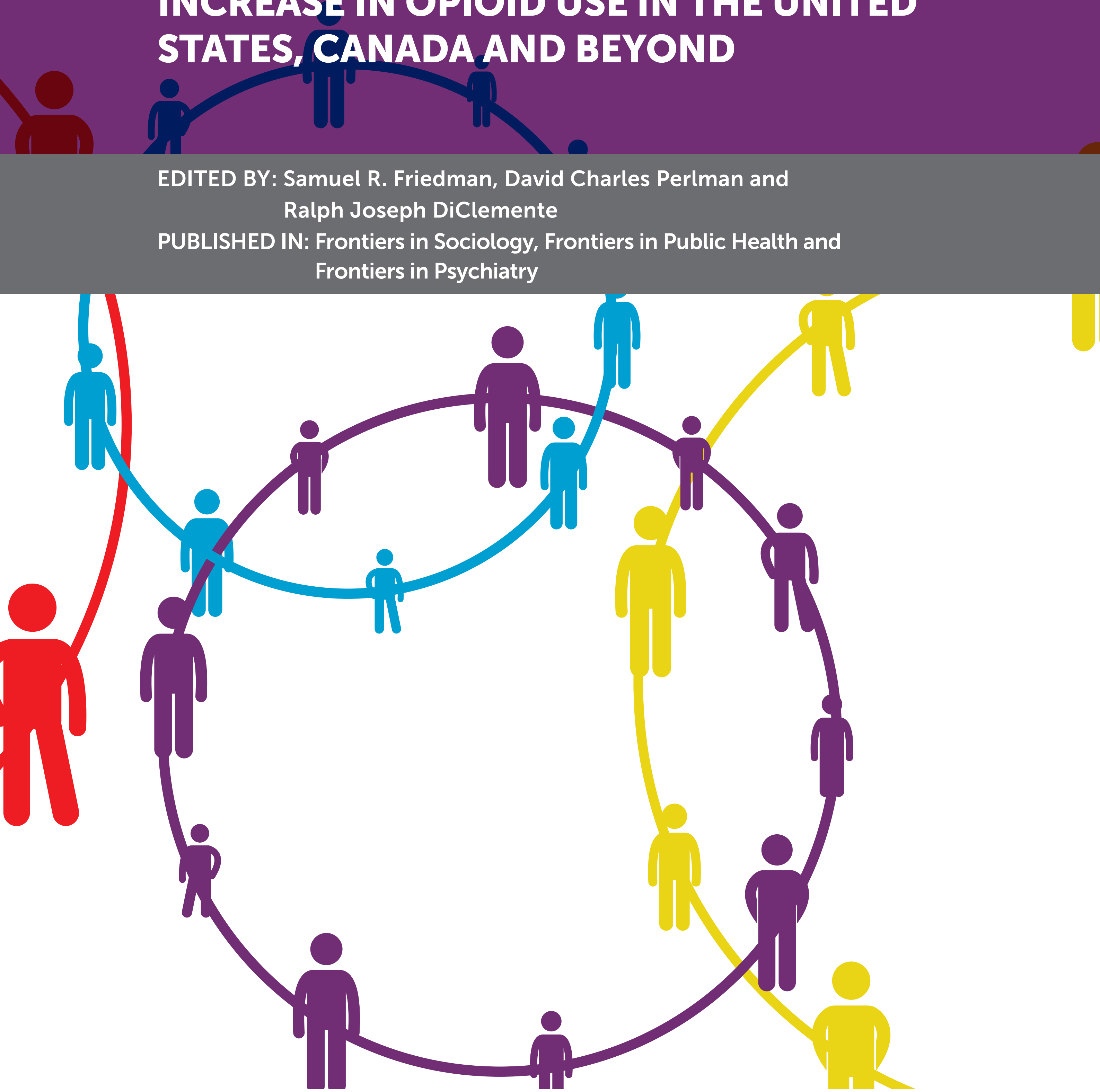

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THE OUTBREAK AND SEQUELAE OF THE INCREASE IN OPIOID USE IN THE UNITED STATES, CANADA AND BEYOND

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Editorial: The outbreak and sequelae of the increase in opioid use in the United States, Canada, and beyond

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Editorial on the Research Topic
The outbreak and sequelae of the increase in opioid use in the United States, Canada, and beyond

In 2018, there were 67,367 drug overdose deaths in the United States, Unfortunately, by 2021, the latest year for which data are available, the number of deaths had increased to over 107,000 deaths. This increase in overdose mortality was probably driven by a combination of upstream processes, most of which derive from ways in which capitalism and its system of nation-states are creating economic and cultural crises. These crises include the COVID-19 pandemic, economic crises, and a deepening culture of despair (Friedman et al., 2021). Relatedly, the illicit drug markets for stimulants and opioids have changed and have come to include widespread highly-potent synthetic opioids (Baldwin et al., 2021). Articles in this special issue provide insights into existing and potential strategies to prevent risky opioid use and reduce opioid mortality. We briefly discuss each of the articles in this issue and highlight key ideas, constructs, and recommendations for research and intervention.

Friedman et al. present evidence that the opioid/overdose epidemic is not only a question of individual behaviors—although those are important—nor only of corporate greed in the over-zealous marketing of dangerous opioids as harmless pain medicines, but that the overdose epidemic is part of a deeper dialectic of one-sided class war, the impacts of economic trends on profits, wages, employment, wealth and housing inequality, and of the associated social, community, ideological and psychological changes these cause.

The recent changes in the racial/ethnic distributions of overdose mortality suggest that the processes discussed in the Friedman et al. paper have taken place in a deeply racialized society where economic, political, and ideological changes are shaped by, and in turn shape, patterns of oppression and of struggle (Friedman et al., 2022b).

Bergo et al. extend prior work by Van Handel et al. (2016) using area-level measures of several syndemically related processes to predict the *need* for overdose, HIV, and hepatitis C prevention. Lyss et al. present evidence that the CDC county vulnerability index has not been an effective predictor of HIV outbreaks. Bergo et al. add new measures to create a revised index and examine ecologic associations at the ZIPCODE rather than county level, permitting greater geographic precision. One research question raised by this paper is whether indicators of a locality's "need" for overdose interventions are actually associated with whether interventions are implemented and/or their scale. Research on the placement and magnitude of syringe service and drug treatment programs across metropolitan areas suggests that associations between "program need" and "program implementation" have been weak at best (Friedman et al., 2007; Tempalski et al., 2007, 2008). Similarly, further research is needed on whether localities that need overdose programs the most are those where interventions are likely to be most effective. Recent experience in the United States, where some States or other localities with particularly severe COVID-19 epidemics have rejected mask mandates (and have had a low response to voluntary masking) and/or have responded poorly to vaccination campaigns exemplify that need may not predict either the existence or effectiveness of programmatic responses (Kahane, 2021; Kelman, 2021; Sehgal et al., 2022).

Gaps between need and effective response may also interact with programs of stigmatization of people who use drugs, particularly since drug policy has long been racialized in the United States and this is likely to interact with trends for overdose mortality to become more associated with racially-oppressed minorities (Friedman et al., 2022a; Kiang et al., 2022; Townsend et al., 2022).

Treatment for opioid use disorder, particularly *medications for opioid use disorder (MOUD)* in the United States is sometimes pointed to as the key route to ending opioid-related overdoses and related mortality. Such suggestions, however, seem incomplete given the currently-limited population-level effectiveness of MOUD. As discussed in Williams et al. (2019), OUD treatment is inadequate in the US: Of the 2.1 million people who are estimated to need care, approximately 20% are receiving treatment, and only 35% of these are receiving FDA-approved medications (methadone, buprenorphine, extended-release naloxone). Furthermore, retention in treatment programs for 6 months or more is low, and long-term "remission" is even lower. Thus, getting enough people at risk for overdose into treatment will require a large increase in available treatment and an increase in the proportion who receive evidence-based treatment (MOUD). Once in treatment, however, the prospects for retention are low, and for a cure even lower. Thus, to have a substantial impact on the opioid/overdose crisis, treatment would need large increases in the number, geographic distribution, insurance coverage, quality, patient satisfaction, retention, and overall improvements in efficacy and population-level effectiveness.

In sum, then, the articles on treatment in this special issue by Blazes and Morrow, Mistler et al., and Frank and Walters offer useful, though insufficient, contributions to improving the opioid/overdose crisis. Population-level improvements will likely require implementing "upstream" interventions plus effective community-level interventions.

Blazes and Morrow address the co-formulation of buprenorphine and naloxone. The rationale for co-formulating these agents was to prevent the diversion of buprenorphine prescribed as MOUD to illicit injection use. Including naloxone (an opioid antagonist) with buprenorphine blunts the opioid effects, possibly (perhaps probably) reducing overdose and, by reducing euphoria when injected, possibly reducing incentives for diversion. The authors point out that this formulation has not consistently deterred its diverted use or misuse; this is confirmed by the observation that injection of buprenorphine-naloxone formulations is prevalent and, in some jurisdictions, is the most prevalent form of illicit drug injection (Johnson and Richert, 2019). Further data on the impact of this co-formulation on population-level overdose rates are needed.

Mistler et al. highlight that cognitive dysfunction, of various etiologies, can prevent achieving effective intervention outcomes to address the harms of opioid use. They suggest that for PWUD who enter methadone treatment, it is important to develop more effective ways of recognizing and addressing mental health disorders Based on two focus groups with providers and patients from one MMTP, they suggest ways to achieve this.

Frank and Walters conducted qualitative research with MOUD patients and treatment providers and showed that many patients enter MOUD not because they want to, but rather because they experience constrained choices attributable to drugs' illegality; peer and family pressure; fear that authorities seize custody of their children; and/or because of internalized stigma. Analyses of patients and their interaction with providers, however, often assume that patients are in treatment voluntarily, and treatment decisions are often made on that basis. Frank and Walters suggest that recognizing the often-coercive context of treatment-seeking may provide insights for providers and people in treatment to develop more productive interaction strategies. Further research is necessary to assess whether improved interaction results in reducing overdose mortality in the absence of changing the broad upstream, oppressive context.

Other papers in this issue lay the basis for community-level interventions. Some of these, such as Bagchi et al., Riazi et al., and Des Jarlais et al., approach this through community education and/or counseling. Ellis et al. suggest both educational interventions and changing the ways authorities respond to PWUD.

Bagchi et al. view opioid overdose, hepatitis C, and HIV as a syndemic that requires integrated interventions that incorporate consideration of each condition, and also suggest the need for interventions addressing broader underlying forces that increase risk; such as stigma, structural vulnerability, and siloed systems of care. They describe a 90-min Structural Competency Curriculum to train primary care providers. The limit of 90 min is realistic, since US health care focuses on high-profit individual care, even though it is widely recognized that addressing 'upstream' social and structural determinants is crucial. Provider-level interventions are also self-limited. At best, they lead to better awareness and practice in patient-provider interactions, but this cannot change in oppressive structures that underlie the opioid epidemic.

Riazi et al. describe an innovative program to provide overdose education and naloxone distribution training to at-risk populations and bystanders so that overdoses can be reversed. The program was implemented at public events, community-based organizations, substance use programs, educational facilities, homeless prevention programs, faith-based organizations, and alternatives to incarceration programs. It also used a train-the-trainer model to teach medical students and nurses to train others in these techniques. This article also provides useful information about how they adapted this program during the COVID-19 initial emergency period.

Des Jarlais et al. present a model of how some people who inject drugs come to initiate other PWUD into injecting (which is associated with a higher risk of infections and overdose). The stages in this process are promulgating positive visions of injection drug use; being asked to initiate by someone, and then initiating. It has long since been proposed that harm reduction efforts might work with potential initiators to keep them from initiating others or, at least, convince them to model safer injection techniques (Hunt et al., 1998). Des Jarlais and his collaborators have developed a "Break the Cycle" intervention to locate likely initiators and train them not to initiate others. This intervention seems to reduce the extent to which such initiators initiate others into injection (Des Jarlais et al., 2019; Uusküla et al., 2022).

This is a promising intervention, but several important questions remain to be answered: 1. Do those PWUD who ask to be initiated find other people to initiate them? 2. Of those who do not, how many initiate without the assistance of an experienced injector? 3. Does the experience of being refused by a potential injector, or of being unable to find one, reduce the subsequent probability of overdosing, dying from an overdose, or becoming infected among PWUD who asked? 4. Does implementing the Breaking the Cycle intervention in a locality or in a social network of PWUD reduce the rate of initiating injection and/or overdose in that locality or network?

Ellis et al. studied the healthcare experiences of PWUD in rural Southern Illinois qualitatively. Participants reported several ways in which their treatment dissuaded them from using medical services. These included forced catheterization, divulging drug test results to law enforcement, sharing details of counseling sessions with community members, and fear of calling emergency services if someone had an overdose. They suggest reforming and clarifying law enforcement's role in Emergency Departments, instituting diversion policies during arrests, stigma training, and harm reduction education for emergency medicine providers, and referral systems between Emergency Departments and local harm reduction agencies. These suggestions have some basis in practical experience and in theory, but research is needed to see if they can restore PWUD's trust in medical services and, in particular, if such efforts can reduce fatal overdoses.

Ventuneac et al. and Guarino et al., focus on the epidemiology of risk.

Ventuneac et al. show that people living with HIV disproportionately use opioids. To some extent, this may be attributable to HIV acquisition through high-risk injection or sexual practices. In addition, some people living with HIV have had periods of severe pain due to HIV-associated complications or morbidities, which may lead to drug initiation, dependency, and overdose risk.

Guarino et al. studied a group of community-recruited young adult (aged 18–29) opioid users to assess the association of childhood traumatic events with the age of initiation of seven different drug behaviors. They observed that the more types of childhood traumatic events participants experienced, the earlier the age at which they underwent each kind of drug use initiation. This suggests that childhood trauma may contribute to vulnerability to high-risk drug use. A cohort study could provide additional information about these relationships.

What is not clear, in the context of 40 years of increasing overdose mortality in the United States (Jalal et al., 2018), which during some periods has been closely tied to increasing opioid use, is whether the increase in opioid use and/or overdose mortality at the population level is, in part, caused by increases in childhood trauma. It is certainly plausible, for example, that the one-sided class war described by Friedman et al. could engender family and individual stressors among adults that would, in turn, lead to increases in childhood trauma. Greater understanding of this pathway, and its prevalence, may point the way to developing innovative prevention methods that intervene against overdose mortality by an upstream approach to reducing childhood trauma.

Many of the research and innovative proposals discussed in these papers concern upstream interventions or expanding and improving existing harm reduction and treatment efforts. Although no papers focused on these, we would also suggest ensuring a safer drug supply may reduce the overdose risks from synthetic opioid adulterants. Additionally, repealing the criminalization of drug use may lead to greater drug treatment seeking, reduced stigma, and, as a consequence, less opioid-associated mortality. Given the scope of the opioid crisis, we would urge expanded effort to develop, implement, and evaluate innovative strategies, community partnerships, and public health policies.

Author contributions

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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A Structural Competency Curriculum for Primary Care Providers to Address the Opioid Use Disorder, HIV, and Hepatitis C Syndemic

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The interrelated epidemics of opioid use disorder (OUD) and HIV and hepatitis C virus (HCV) infection have been identified as one of the most pressing syndemics facing the United States today. Research studies and interventions have begun to address the structural factors that promote the inter-relations between these conditions and a number of training programs to improve structural awareness have targeted physician trainees (e.g., residents and medical students). However, a significant limitation in these programs is the failure to include practicing primary care providers (PCPs). Over the past 5 years, there have been increasing calls for PCPs to develop structural competency as a way to provide a more integrated and patient-centered approach to prevention and care in the syndemic. This paper applies Metzel and Hansen's (1) framework for improved structural competency to describe an educational curriculum that can be delivered to practicing PCPs. Skill 1 involves reviewing the historical precedents (particularly stigma) that created the siloed systems of care for OUD, HIV, and HCV and examines how recent biomedical advances allow for greater care integration. To help clinicians develop a more multidisciplinary understanding of structure (Skill 2), trainees will discuss ways to assess structural vulnerability. Next, providers will review case studies to better understand how structural foundations are usually seen as cultural representations (Skill 3). Developing structural interventions (Skill 4) involves identifying ways to create a more integrated system of care that can overcome clinical inertia. Finally, the training will emphasize cultural humility (Skill 5) through empathetic and non-judgmental patient interactions. Demonstrating understanding of the structural barriers that patients face is expected to enhance patient trust and increase retention in care. The immediate objective is to pilot test the feasibility of the curriculum in a small sample of primary care sites and develop metrics for future evaluation. While the short-term goal is to test the model among practicing PCPs, the long-term goal is to implement the training practice-wide to ensure structural competence throughout the clinical setting.

Keywords: structural competency, syndemic, curriculum, primary care, opioid use disorder, HIV, hepatitis C

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INTRODUCTION

In 2017, an estimated 47,600 Americans died from opioid overdoses, representing 67.8% of all drug-related overdose deaths that year (2). Vital statistics demonstrate significant overlap in the opioid misuse epidemic with infectious disease outbreaks, with the most recent estimates suggesting that ∼67% people who inject opioids are infected with the hepatitis C virus (HCV) and 33% with HIV (3, 4). Furthermore, in the 2014–2015 HIV epidemic in Scott County, Indiana, among the 181 people newly diagnosed with HIV, 88% had injected oxymorphone and 92% were co-infected with HCV (5).

These interrelated and synergistic relationships between epidemics has been defined as a "syndemic," (6) reflecting temporal, geographical, and biological interactions between the individual disorders. The syndemic of opioid use disorder (OUD) and overdose, HIV infection, and HCV infection (hereafter, "the syndemic") has been appropriately identified as one of the most pressing public health issues facing the United States today (7). As Milstein has described, addressing this, or any syndemic, requires prevention, and treatment of each individual problem, as well as "the forces that tie those diseases together" [(8), p. 2]. Chief among these is the need to combat structural stigmas that have led to siloed and inefficient systems of care (e.g., specialty addiction treatment facilities to manage OUD, infectious disease [ID] specialists/the Ryan White HIV/AIDS Program for HIV, and gastroenterology/ID to manage HCV and associated chronic liver disease).

While Goffman (9) is generally cited as providing the earliest treatise on stigma, more recent theorists have expanded on his original ideas to advance a more nuanced understanding of how stigma operates in the United States (9). The model of Link and Phelan (10) is particularly suitable for understanding the syndemic because it identifies labeling, stereotyping, prejudice, and discrimination as the major components of stigma, but also highlights the role that power plays in perpetuating stigma (10). In this conception, societal structures (e.g., economic, social, political, and historical systems) create inequitable systems of power that enable expressions of stigma, which then create and sustain health inequities. As such, eliminating stigma requires moving beyond individual-level interventions (e.g., behavioral treatment for substance use disorder and reducing rates of opioid prescribing) to higher-level disruptions in systemic and structural factors that perpetuate health inequities.

The Role for Primary Care Providers (PCPs)

A commonly-cited barrier to addressing the syndemic has been the lack of access to prevention and treatment services (11–14). Estimates suggest that among the 22 million people in need of addiction services, only 11% have access to specialty care and, among those with OUD, almost 80% lack access to treatment (11, 12). In the HIV epidemic, despite long-standing recommendations from the CDC that all individuals ages 13–64 receive an HIV test (15) only 40–46% of adults have ever received one (16, 17) and, in 2018, only 8.1% of individuals at high-risk for infection received pre-exposure prophylaxis (PrEP) (18). Finally, the CDC estimates that nearly 2.4 million people are living with HCV in the United States and notes that the cost of treatment has led to underutilization of curative therapy (19). The United States Preventive Services Task Force (USPSTF) recently posted updated recommendations for HCV testing (20). The previous recommendation was that all adults born between 1945 and 1965 be screened for HCV, but the new guidelines suggest screening for all adults ages 18–79. Although there have been successful models of care integration for management of HIV and OUD, these have largely been in specialty care settings and there has been inadequate uptake in primary care practices (21). Similarly, while there have been successful models of HCV integration into primary care (22–24), including increasing consideration for OUD (25), such comprehensive approaches remain underutilized.

As a way to address the opioid overdose epidemic, several state- and federally-funded initiatives have focused on more responsible opioid prescribing among primary care providers (PCPs), including daily limits on milligrams of morphine equivalents (MME) and mandatory consultation of prescription drug monitoring program (PDMP) databases. However, as Dasgupta et al. (26) note, these approaches ignore institutionalized racial biases (e.g., laws that have criminalized drug use by members of ethnic minority groups as reflecting individual decision-making and "moral failures") and structural factors (e.g., poverty and limited social capital) that underlie components of the syndemic (26). In addition, these opioid-specific approaches perpetuate the siloed nature of health services and fail to take the type of integrated approach that is needed to combat the syndemic. For example, the focus on opioid-related overdoses frequently overlooks other co-occurring substance use disorders, such as injection of methamphetamines, which also contributes to increase risk for HIV/HCV and overdose risks associated with polypharmacy (e.g., opioids and sedatives or stimulants) (27–30).

Providers in primary care settings (e.g., private practices, federally qualified health centers, and retail clinics) are uniquely positioned to offer comprehensive, patient-centered care that can accommodate individual needs. Greater incorporation of guideline-based screening into existing care and services will allow practicing PCPs to address service gaps without necessitating significant changes in clinic workflow or operations (14). Most importantly, by normalizing prevention and treatment services in primary care settings, the healthcare system can begin to address the stigma that underlies the critical intersection of the disorders within the syndemic. In general, PCPs can take a more active role in addressing structural stigmas and there have been increasing calls over the last 5 years for PCPs to develop structural competency as a way to provide a more integrated and patient-centered approach to prevention and care in the syndemic (1, 7, 31, 32). In particular, structural competency is seen as a way to address the institutionalized factors that shape social responses and clinical interactions (1). Recent reviews highlight successful office-based models for treatment of substance use disorders, which can be modified to address structural factors fueling the syndemic (13, 21, 33). For example, harm reduction programs and medication for addiction treatment (MAT) promote a patient-centered approach to treatment that shows promise for overcoming barriers associated with socioeconomic status, institutionalized racism in the criminal justice system, and stigma.

The Model for Structural Competency Training

In their seminal paper, Metzel and Hansen (1) defined *structural competency* as "the trained ability to discern how a host of issues defined clinically as symptoms, attitudes, or diseases … also represent the downstream implications of a number of upstream decisions" related to public policies, supply chains operating within the healthcare system, and even "the very definitions of illness and health" (32, p., 5). The authors propose the need to expand traditional models of "cultural competency" into an educational approach that recognizes, and seeks to interrupt, these long-standing interactions, which perpetuate stigma and social inequality. As with the construct of "cultural humility," (34) structural competency is understood not as an endpoint denoting mastery, but as a process of genuine self-reflection and recognition.

"Recognizing the Structures that Shape Clinical Interactions" (32, p. 6)

Metzl and Hansen (1) described five skill-sets to form the basis for a structural competency curriculum for health care professionals (1). The first calls on clinicians to recognize the ways in which patient-provider interactions operate as functions of structural vulnerability. When a patient presents with poorly controlled diabetes, providers may assume that the patient (a) is reluctant to exclude "culturally preferred" foods from their diet (b) needs additional education on insulin administration, or (c) simply lacks the motivation to participate in recommended physical activity. Indeed, guidelines for management of such chronic conditions as diabetes and hypertension highlight "lifestyle changes" as the preliminary approach to management. However, such assumptions overlook factors associated with inadequate access to fresh foods and unsafe neighborhoods that restrict opportunities for daily exercise. While there is increasing awareness of these social determinants of health, structural factors, such as the pressure to conform to a 15-min encounter or the policies related to drug reimbursement, while recognized, go relatively unchallenged. It is important for clinicians to recognize that the social determinants of health may be the factors that contribute to disparities, but it is the structural conditions within society that explain why and how these factors lead to health inequities (35).

A common barrier to guideline-based screening in primary care settings is a belief that incidence of a given condition (e.g., HIV) is low in the provider's service area (36). Such attitudes perpetuate the ineffective, siloed approach to primary care practice. Van Handel et al. (37) found that six factors of structural vulnerability are predictive of the risk for syndemic outbreaks within a given geographic area (37). Specifically, these indicators include (a) the overdose death rate; (b) the number of prescription opioid sales; (c) the capacity for buprenorphine administration, as evidenced by the number of providers with a Drug Addition Treatment Act of 2000 (DATA 2000) waiver; (d) the percentage of non-Latino white residents; (e) per capita income; and (f) the unemployment rate. PCPs should consider these broader conceptions of risk in the provision of preventive services, including screening for HIV and HCV among patients receiving opioid prescriptions.

"Developing an Extra-clinical Language of Structure" (32, p. 7)

The second skill of Metzel and Hansen's (1) framework challenges PCPs to consider structural barriers from the perspective of other disciplines (e.g., psychiatry, public health, sociology, and anthropology) (1). Abundant evidence documents ethnic health disparities in infant mortality rates, obesity, and cancer screening (38–40). However, a structurally competent approach explores the nature of these disparities in their historical, economic, and sociological context. For example, Ransome et al. (41) explored the structural factors leading to late presentation for HIV testing (i.e., when infection has already progressed to AIDS) in communities with high concentrations of African American residents (41). These authors found that high socioeconomic deprivation and access to testing services did not mediate the association. They suggested the need to consider patterns of marriage/sexual partnerships and disproportionate incarceration rates as factors underlying diagnostic disparities.

"Rearticulating 'Cultural' Presentations in Structural Terms" (32, p. 9)

The third skill in Metzel and Hansen's framework requires providers to reframe "cultural differences" in terms of structural explanations (1). In their various publications, Metzl and Hansen draw a clear distinction between cultural and structural competency. They describe cultural competency as a process that operates at the individual level to identify clinicians' biases and to enhance patient-provider communication (42). Structural competency, on the other hand, is a method of integrating explanatory frameworks from multiple disciplines to identify higher level sources of health inequities (42, 43).

In a clinical scenario they present, Metzl and Hansen (1) describe Mrs. Jones as "an African American woman in her mid-60s who comes late to her office visit and refuses to take her blood pressure medications as prescribed" (32, p. 2). Under a cultural competency framework, the clinician may see the patient's ethnicity as a source of greater susceptibility to hypertension. The fact that she "comes late" to her appointment could be dismissed as a cultural proclivity against the value of timeliness. Finally, her "[refusal] to take" her prescribed medications may indicate to the clinician a need to provide more patient education regarding the effects of hypertension on critical organ systems and the importance of medication adherence for maintaining a healthy blood pressure. While it is important not to discount such factors in a clinical encounter, a structurally competent approach would consider, for example, how systemic structural racism can lead to a sense of hypervigilance among members of ethnic minority groups and that such a constant state of awareness leads to stress, which can in turn lead to increased blood pressure levels. The structurally competent approach moves beyond "genetic" and individual factors and considers how society operates to reinforce racial injustice.

"Observing and Imagining Structural Intervention" (32, p. 10)

In the traditional approach to care, clinicians would consider the case of Mrs. Jones and might provide her with a pill organizer or set up text or telephone reminders for her to take her medications. Most primary care practices abound with patient-facing educational brochures to explain common, chronic health conditions and how to better manage them. However, a structurally competent approach to care requires creativity and a willingness to disrupt long-standing assumptions about what is possible in clinical care (Skill 4). As Metzl (44) eloquently put it, structural forces should not be seen as "immutable or beyond the reach of intervention or repair" but as "stories" that are "subject to revision through imagination, reparation, and transformation" (44, p. 217). As Metzl and Hansen (1) point out, Dr. Jack Geiger started prescribing food as a health intervention in the 1960s (45). At the time, such an approach was seen as unusual and impractical. Today, food prescriptions have become a common practice for managing obesity, hypertension, and diabetes (46).

"Developing Structural Humility" (32, p. 12)

The final component to a structurally competent approach is developing an openness to a patient's evolving narrative (1). The American Academy of Pediatrics is credited with coining the concept of the patient-centered medical home in 1967 and "patient-centeredness" has been an idealized notion in the healthcare system for the past 50 years (47). However, it is rare to find a health care delivery system that treats the patient as a true co-equal collaborator in their own care. Many people who have served as the health caretaker of someone unable to speak for themselves can relate to the experience of being dismissed by a member of the medical establishment (i.e., "We can't find anything wrong with your son/mother/brother/etc."). However, the caretaker often knows when their loved one is "not acting right." A clinician taking a structurally competent approach solicits the patient/caregiver's insights as a co-equal "expert" on the patient's condition as part of everyday practice.

According to Montoya (48), there are four keys to structural humility (48). The first reflects this view of patients as authorities and calls on clinicians to ask "real questions," ones "for which you do not already have an answer" (48, p. 153). For example, Kleinman's Explanatory Models Approach (49) solicits the patient's narrative (e.g., "What do you call this problem?," "What do you believe is the cause of this problem?"), rather than simply accepting the biomedical model, which assumes the provider already knows the answers relating to the problem's description and etiology. The second is to embrace discomfort. In describing Yale's Department of Psychiatry Structural Competency Community Initiative (YSCCI), Rohrbaugh et al. (50) described the discomfort program participants felt when members of the local community criticized Yale University's treatment of them as mere subjects for study (50). A structurally humble approach acknowledges the legitimacy of these perspectives and takes them into consideration when developing interventions. Montoya's third recommendation is for clinicians to be willing to admit that they do not know everything (i.e., "Be someone you'd like to know" (48, p. 153). This includes knowledge of oneself, not just one's implicit biases (51) but the various types of privileges that shape one's interactions with the world (52, 53). Finally, Montoya encourages clinicians to see their patients as more than just the problems they face (48). This means acknowledging the abilities that patients have in contributing to their care.

Pedagogical Frameworks for a Structural Competency Curriculum

The proposed curriculum and its delivery draw on concepts from culturally relevant pedagogy (CRP) (54) and adult learning theory (55). Ladson-Billings developed CRP as an approach that draws on the cultural diversity of learners as a strength in the learning process, which helps to build "academic success," "cultural competence," and "sociopolitical consciousness" [(56, 57)—p. 75]. While generally grounded in a formal educational setting, the theoretical underpinnings of CRP are relevant in the clinical encounter since a critical role of clinicians is to provide patient education. When delivered in the context of a hierarchical relationship, such education is seldom effective because, in a structural competency framework, health is about more than individual behavior. When health care providers are made aware of the power differentials within the patient-provider relationship, they can approach patient education as an opportunity for mutual learning. Recognizing and incorporating the patient's lived experience in their delivery of services raises the social consciousness of health care providers beyond the immediate encounter.

As described in detail in the sections that follow, the approach to instruction presented here challenges practicing clinicians across the six domains of the andragogical framework (55). First, through didactic instruction, providers will gain a greater understanding of the importance of addressing the structural barriers their patients face to achieving optimal health outcomes. The content of this didactic training was recently delivered to an interdisciplinary group of graduate students participating in a Health Resources and Services Administration-funded program on the management of OUD in primary care (see **Presentation 1** in **Supplementary Material**). Second, because the majority of practicing clinicians are unfamiliar with the concept of structural competency, the curriculum will encourage them to re-assess their awareness of the challenges their patients face. Third, by drawing on commonly encountered clinical challenges, providers will be able to contrast their own experiences with more comprehensive approaches to patient care. Fourth, the use of case studies will provide an opportunity to reflect on their readiness to manage the care of patients affected by the syndemic. Fifth, a structurally competent approach necessarily requires health care providers to re-orient their approach to care within broader societal structures. Finally, practice with the administration of structural vulnerability assessments will offer learners the opportunity to examine the quality of the questions they pose within the clinical encounter.

THE LEARNING ENVIRONMENT AND EDUCATIONAL FORMAT

A recent body of work has described structural competency training programs within medical schools, including training for pre-health/pre-med students, medical residents, and students of psychiatry (42, 43, 52, 58, 59). As described in Hansen and Metzl's (59) compendium of case studies, these efforts represent a small, but growing, number of interdisciplinary programs designed to bring awareness of structural influences on health into formal medical training programs (59). However, what is lacking is a training program that can address the knowledge and skills gaps of practicing providers. In the time-pressured environment of primary care, providers are unlikely to be willing to take the time to participate in tours of their surrounding communities to better understand the structural factors contributing to the challenges their patient's face in managing their health. However, it is critical to increase awareness of structural competency as a way to combat stigma in the syndemic and develop a more integrated approach to the provision of preventive and treatment services.

The goal of this section of the paper is to apply Metzel and Hansen's (1) five-part framework for improved structural competency in the design of a targeted educational curriculum on the syndemic that can be delivered on-site to practicing PCPs and their staff members (1). The proposed curriculum (**Table 1**) includes didactic lectures, interactive activities, case studies, discussions, individual practice assessment, and brainstorming. Altogether, the training is designed to take one and a half hours (i.e., 15 min to cover components 1 through 3 and 5 and 30 min to identify practice-specific interventions). Ideally, the training session will be followed with 3–6 monthly consultations to assist practices to implement workflow changes, applications, and other changes identified in the interventions phase. The objective is to test the feasibility of the program in a small sample (i.e., 3–5 practicing PCPs) and develop appropriate metrics to evaluate the model and refine it for further testing.

Recognizing Structural Vulnerability in the Syndemic

The first phase of the proposed curriculum involves a didactic presentation that explores the constructs of structural competency and contrasts them with those of cultural competency and the social determinants of health (see

TABLE 1 | Structural competency curriculum for addressing the syndemic in primary care.

Module number/topic	Time (mins.)	Activities	Mode(s) of instruction
1. Recognizing structural vulnerability in the syndemic	15	Didactic presentation - topics:[a] • What's a syndemic? • Pharmaceutical companies' role in the opioid epidemic ○ Marketing of opioid medications ○ Understatement of opioid addictive potential • The War on Drugs and mass incarceration • The Ryan White HIV/AIDS Program • Federal funding priorities and HIV/HCV • Stigma's role in the syndemic	• Presentation • Group discussion
2. Taking a multidisciplinary approach to structural vulnerability	15	Discussion of tools for assessing vulnerability: • Social isolation as a risk factor in the syndemic ○ UCLA Loneliness Scale (60) • Defining structural vulnerability ○ Structural Vulnerability assessment (61)	• Self-assessment • Group discussion
3. Structural explanations in case studies	15	Case Studies in Social Medicine - from *The New England Journal of Medicine*: • "The Structural Violence of Hyperincarceration — A 44-Year-Old Man with Back Pain" (62) • "Structural Iatrogenesis—A 43-Year-Old Man with 'Opioid Misuse"' (63)	• Group discussion
4. Structural Interventions	30	Practice assessment and brainstorming: • Review of tools for HIV/HCV/OUD screening • Process for applying for a DATA 2000 waiver • Using the PDMP for medication management • Identification of referral sources practice is currently lacking • Review of patient education relating to safe use, storage, and disposal of opioid medications	• Small group brainstorming • General discussion
5. Structural humility	10	Identity Wheel exercise (53)	• Self-assessment • Group discussion
6. Wrap up and next steps	5	Identification of additional resources/training needed for individual providers and the practice as a whole - possible examples: • Screening and Brief Intervention (SBI) for OUD (13) • Clinical protocols for management of HIV/HCV/OUD • Contingency management in the syndemic	• Individual practice assessment • Brainstorming • Group discussion

[a] *See **Presentation 1** in **Supplementary Material**.*

Presentation 1 in **Supplementary Materials**). During this time, we will also provide an overview of the historical and social precedents (particularly stigma) that created the siloed systems of care for OUD, HIV, and HCV. This review will start by defining the syndemic and describing the interactions between the three conditions, as well as risks imposed by co-occurring substance use disorders. The presentation will include discussions of the role of pharmaceutical companies in marketing opioid medications to prescribers and minimizing the addictive potential of these drugs, as well as the racial implications of the "War on Drugs" and mass incarceration (26, 59, 64). It will provide a brief history of the Ryan White HIV/AIDS Program and the failure of the federal government to prioritize funding for the development of pharmaceutical treatments for HIV and HCV (65, 66). Finally, this segment of the curriculum will review Link and Phelan's model of stigma (10) and identify how integration of care for the syndemic within primary care practices can help to better integrate services and reduce syndemic-related stigma.

Taking a Multidisciplinary Approach

Recent studies suggest that loneliness is prevalent throughout U.S. society (67–69). A study that used the University of California—Los Angeles's Loneliness Scale found that 46% of Americans report feeling alone at least some of the time (70). The study further indicated that, rather than alleviate the sense of loneliness, heavy use of social media is associated with a greater sense of loneliness (i.e., 73% of heavy social media users reported feeling alone vs. 52% among light users). During the second portion of the training, participants will review the Loneliness Scale (60) and will discuss the implications of loneliness on coping patterns (e.g., loneliness as an etiological factor contributing to substance misuse as a coping mechanism) and social engagement.

During this portion of the training, we will also present the Structural Vulnerability Assessment Tool developed by Bourgois et al. (61). The tool includes questions related to 8 structural dimensions (e.g., financial security, residence, risk environments, etc.), along with specific follow-up questions for each. For example, the question relating to residence asks, "Do you have a safe, stable place to sleep and store your possessions?" Follow-up questions include "How long have you lived/stayed there? Is the place where you live/stay clean/private/quiet/protected by a lease?" (68, p. 15) We will review the tool and talk about the practice's readiness to incorporate the items in health assessments.

Identifying Structural Explanations for Health Outcomes in the Syndemic

In its Perspective section, the *New England Journal of Medicine* has a regular feature called "Case Studies in Social Medicine." These articles highlight real cases and examine the structural implications inherent in patients' interactions with the health care system. During this section of the training, participants will review up to two cases relating to patients with complaints of chronic pain and examine the traditional approach they would take to these cases vs. one that considers structural factors. One goal will be to discuss how structural factors are frequently seen as cultural representations. The emphasis will be on understanding how to break down stereotypes to identify the structural forces that create risks and barriers that cross ethnic and socioeconomic lines.

Implementing Structural Interventions in Primary Care

Because the goal of the training is to motivate providers to implement changes in their practice, the training will include 30 min to discuss specific structural interventions that practices can implement to address the syndemic. Specifically, we will first assess the extent to which practices are engaging in routine HIV, HCV, and OUD screening according to guidelines; implementing harm reduction interventions (e.g., prescription of PrEP and naloxone distribution); employing prescribers with DATA 2000 waivers to prescribe buprenorphine for OUD; and using the State PDMP for prescription opioid management, particularly among patients with infectious diseases. To the extent that practices do not have these systems in place, or are not using them efficiently, we will provide information, training, scripts, and tools to facilitate their uptake. Based on the prior discussions, we will also review the practice's list of referral sites and identify gaps in services for which new sites of referrals can be developed. Finally, we will review the practice's educational initiatives relating to the safe use, storage, and disposal of opioid medications and will ensure that sites have a list of local disposal sites of opioid medications and information that they can provide to patients regarding when and how to dispose of medications safely when there are no local drop-off sites available. The goal will be to help practices develop a more integrated system of care that can overcome clinical inertia for managing the syndemic.

Approaching the Syndemic With Humility

The last portion of the training will focus on recognizing privilege as a component of structural humility. We will use an abbreviated version of the Identity Wheel exercise described by Chow et al. (53). The activity involves participants filling out two rings of a circle, one which includes given identities (e.g., age, nationality, language) and the other that includes chosen identities. After participants fill out their wheels, they engage in directed discussions regarding the meanings of their social identities. The goal is for participants to understand that there are identities that are salient to others that are not as relevant to their own experiences. Under the original model, the activity is expected to last at least 40 min. Due to time constraints, the activity for this training will focus on a shortened list of discussion questions, specifically, those focusing on identities that privilege providers in their professional roles and how these experiences differ from those of their patients.

Program Wrap Up

The final portion of the program will focus on lessons learned and next steps. As prior researchers have noted, there are many successful models of primary care, office-based management for intersecting disorders (13, 33). However, approaching care within the syndemic requires an individualized approach that addresses the strengths and needs of the specific clinical practice site (33). As such, the final 5 min of the training will involve a summary of lessons learned and identification of additional training that individual clinicians may need, or workflow processes that need to be revised at the practice level.

Approach to Assessment

Assessment of participant learning will be based on Bloom's Taxonomy (71). Specifically, we will focus on the knowledge, skills, and attitude domains. Specially, for the knowledge domain, we will assess participants' ability to apply concepts of structural competency in their discussions of the case studies. Through this activity, participants will be able to demonstrate their ability to evaluate their current practice and conceptualize approaches that are more responsive to the structural challenges their patients face. In the domain of skills, participants will have the opportunity to practice data gathering using the Structural Vulnerability Assessment Tool (61) and to adapt the tool to the needs of their practice. Finally, through a post-course evaluation, participants will have the opportunity to reflect on the learning and share their perceptions regarding the utility of the structural competency approach and their intentions to implement changes in their practice.

DISCUSSION

Primary care practices are ideal settings for addressing the syndemic. Evidence shows that many people who inject drugs or are at risk for infectious diseases see their PCPs on a yearly basis but are not engaged in discussions about harm reduction; in many cases, the PCP is not even aware of the patient's risk status (72). Normalizing the management of OUD, HIV, and HCV in the primary care setting can help to reduce the stigma that exacerbates poor health outcomes in the syndemic (13, 21, 73). Until the barriers (including lack of awareness or clinical inertia to prescribe buprenorphine and federal regulations restricting methadone outside of opioid treatment programs) are removed, PCPs should be encouraged to complete training to prescribe buprenorphine and train patients in overdose prevention with naloxone (14, 21, 74). As treatment regimens have become more efficacious and simpler, PCPs should be encouraged to accept the responsibility for medical management of patients with substance use disorder, HIV, and HCV (14, 75). Training in structural competency will help these providers understand that the conditions underlying these intersecting disorders (e.g., stigma, social isolation, and disadvantage) are ideally addressed in settings that promote frequent contact and enhanced trust (13, 14, 26, 32). The goals of the proposed curriculum are 2-fold. First, we seek to expand existing models of structural competency training to target other disciplines, particularly PCPs in active practice. Second, while the proposed training focuses on the theoretical and practical aspects of the syndemic, it also incorporates practical, hands-on activities that can be readily implemented in the busy primary care setting.

The ultimate objective is to deploy and evaluate the training within a sample of primary care practice sites across New Jersey. We expect this to be a multiphase process. The preliminary phase will be a feasibility trial with three to five practicing PCPs to test the content and timing of the various activities. Information gleaned from this trial will be used to refine the content and identify appropriate clinical markers of program efficacy. Obvious objective candidate measures include stigma reduction; number of patients screened for HIV, HCV, and OUD; number of new applications for DATA 2000 waivers; and number of times the PDMP is consulted when prescribing opioid medications. More subjective indicators of program success would include satisfaction with the program and confidence in assessing patients for structural barriers. The long-term goal is to implement the training practice-wide to enhance the structural competency of the entire clinical setting. Eventually, we plan to apply for continuing education credits to implement and test the program across a wide range of practice settings.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Materials, further inquiries can be directed to the corresponding authors.

AUTHOR CONTRIBUTIONS

The author confirms that all work conducted in the development of this paper was solely by AB.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2020.00210/full#supplementary-material

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OPINION
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Reconsidering the Usefulness of Adding Naloxone to Buprenorphine

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INTRODUCTION

We are in the middle of an opioid epidemic with tens of thousands of lives lost every year. As we combat this problem, it is critically important that we continually scrutinize our research efforts and care strategies in the spirit of the scientific method. Especially in light of a death toll that lowered overall US life expectancy for the first time since the flu pandemic in World War I, (1) we must maintain our readiness to reconsider well-established theories and practices in order to improve our efforts to contain this crisis. These efforts will require precision and accuracy in our translation of the literature base. One of the most effective interventions for opioid use disorder has been buprenorphine maintenance therapy, largely using a combination of buprenorphine and naloxone. However, evidence accumulated particularly over the last decade indicates that adding naloxone to buprenorphine may not be as effective a deterrent to misuse by parenteral (i.e., outside the gastrointestinal tract) administration as once thought, and for many patients, naloxone may in fact make the combination product less safe than buprenorphine monotherapy.

Buprenorphine has been used as a monotherapy product since the 1970s. Buprenorphine was combined with naloxone and released as a combination product in the United States in 2002. It was marketed as a sublingual formulation less likely to be abused and injected. This assertion was based on the fact that buprenorphine has relatively high bioavailability with sublingual absorption (35%–55%) compared to naloxone (less than 10%). When administered parenterally naloxone, which is a strong μ opioid antagonist, would be expected to block the partial μ agonist effects of buprenorphine, thereby discouraging such misuse of the product. However, if used as directed the sublingual absorption of naloxone should be less than 10% and, theoretically, not interfere with the pharmacologic actions of buprenorphine. This characterization of the combination product has been generally accepted by the medical community since buprenorphine/naloxone was FDA approved in 2002. This view is reflected in the description of buprenorphine/naloxone products provided by the Substance Abuse and Mental Health Services Administration (SAMHSA) which states, "Because of buprenorphine's opioid effects, it can be misused, particularly by people who do not have an opioid dependency. Naloxone is added to buprenorphine to decrease the likelihood of diversion and misuse of the combination drug product. When these products are taken as sublingual tablets, buprenorphine's opioid effects dominate naloxone and blocks opioid withdrawals. If the sublingual tablets are crushed and injected, however, the naloxone effect dominates and can bring on opioid withdrawals (2)." Based largely on this characterization, it has become the standard of care to use this combination in preference to buprenorphine monotherapy in the United States except in certain special circumstances such as pregnancy.

However, patient experience commonly stands in contrast to the prevalent view of naloxone as a strong deterrent to parenteral misuse of buprenorphine/naloxone products. Many patients with substance use disorders make use of independent, non-evidence based internet harm reduction sites such as "Bluelight" and "Erowid." These are international, online harm-reduction communities, committed to reducing the harm associated with drug use. They host forums and blogs with discussions about patterns and modes of drug use. These sites provide detailed descriptions of pharmacokinetic and pharmacodynamic properties of the substances, and show how this knowledge can be used to maximize the clinical effects of drugs while minimizing potential side effects and withdrawal syndromes. Specific instructions are readily available on these sites for dissolving different preparations of buprenorphine/naloxone and injecting them intravenously. Following these instructions, patients typically experience moderate euphoria and report no symptoms of withdrawal. Such experiences have led to a belief in the drug-using community that the naloxone in these preparations is "inert." We turned to the literature to assess whether there is a scientific basis for this belief, especially since stigma often leads health care professionals to subconsciously discount observations from people with substance use disorders.

Pharmacology

There is pre-clinical evidence to support the claim that naloxone has very limited effects when buprenorphine is present. First, though naloxone can displace most opioids due to its relatively high binding affinity, buprenorphine has a 10-fold greater binding affinity for the μ opioid receptor compared to naloxone (3–5). The slow receptor dissociation kinetics of buprenorphine in conjunction with the rapid elimination kinetics of naloxone further suggests that buprenorphine would largely supplant co-administered naloxone from μ opioid receptors, thus effectively rendering naloxone inert (6). Furthermore, the half-life of naloxone is only 30–40 min. Buprenorphine has a half-life of 24–60 h with other clinical effects such as analgesia and euphoria lasting at least 6 h. Any attenuation of buprenorphine's effects by co-administered naloxone would therefore likely be short-lived. For these reasons, a monograph commissioned by the National Institute on Drug Abuse for exploring the potential of buprenorphine for treatment of opioid dependence recommended against combining sublingual formulations of buprenorphine with naloxone: "Naltrexone, which is approved for maintenance as an oral product, is preferred to naloxone for incorporation into a sublingual buprenorphine product for takehome use. Its duration of action is significantly longer than that of naloxone, more evenly matching that of buprenorphine. Naloxone's short duration of action means that, even if present in substantial dose in the combination, it would only delay the onset of buprenorphine's agonist effects (7)." SAMHSA's clinical guidelines for the use of buprenorphine also state, "Those receiving prescription buprenorphine or buprenorphine/naloxone tablets who dissolve and inject their own medication: This population would experience an agonist effect from buprenorphine but no antagonist effect from naloxone, as large doses of opioid antagonists are needed to precipitate withdrawal in buprenorphine-maintained subjects (8)."

Several clinical studies have demonstrated that parenteral administration of the combined formulation causes precipitated withdrawal symptoms in opioid-dependent subjects (9–11). However, these dramatic consequences only occur under certain specific conditions, namely in subjects who are taking a full opioid agonist such as morphine or hydromorphone and still have significant concentrations of the agonist in their circulation at the time of buprenorphine/naloxone administration. This effect is cited as the main reason naloxone is added to buprenorphine formulation, but the effect is not unique to the combination product. Because it is a high-affinity partial agonist at the μ-opioid receptor, buprenorphine itself will cause precipitated withdrawal in an opioid-dependent person who has a full opioid agonist on board. The presence or absence of naloxone makes little practical difference in this clinical scenario.

Effects on Reward

One of the main findings leading to the conclusion that the combination product has significantly reduced abuse liability is that intravenous naloxone reduces the subjective rewarding effects of buprenorphine. For example, Jones et al. reported in 2017 that naloxone produces an "almost complete attenuation of reinforcing and positive subjective effects" of buprenorphine (12). This reduction of subjective effects has indeed been a consistent finding in multiple clinical studies (12–15), however many of those same studies also showed that the attenuation was only temporary (13, 15, 16). Most subjects report feeling a comparable "high" to buprenorphine alone just 20 to 30 min after co-injection of buprenorphine and naloxone. Though slower pharmacodynamics are known to reduce abuse liability (17), a 20- or 30-min delay in the onset of action is still more than capable of supporting addictive behavior, as evidenced by the widespread abuse of immediate-release oxycodone, whose subjective effects typically peak 1–2 h after ingestion (18).

In any case, multiple lines of evidence have suggested that the subjective effects of drugs are not the primary determinants of their abuse liability. Rather, addictive drug use is driven by a desire to pursue drug-associated rewards that is largely subconscious, sensitizes with repeated drug exposures, and can be entirely dissociated from the pleasurable effects of the drug (19–22). In fact, the pleasurable effects of drugs typically fade away as the user builds tolerance, while the desire to use only grows stronger. The effects of naloxone on actual intravenous self-administration of buprenorphine have been decidedly less clear than the subjective consequences of such use. One study found intravenous self-administration of buprenorphine/naloxone to be statistically lower than that of buprenorphine alone (13), while two other studies from the same group found no statistical difference between the two formulations (12, 15). Empirically, intravenous injection of buprenorphine/naloxone is quite common and documented in the literature (23–28). One study showed that 46% of patients on maintenance therapy (buprenorphine or methadone) have injected buprenorphine intravenously (28).

There is also a recent documented trend to misuse buprenorphine tablets through insufflation (snorting). It is commonly known that naloxone is absorbed readily through intranasal administration. This fact is exploited by the naloxone nasal spray, a single use insufflator used in opioid overdoses. Insufflation provides significantly higher bioavailability for both buprenorphine (up to 48% vs 30% sublingual) and naloxone (up to 30% vs 10% sublingual) (29). Studies of the potential effects of naloxone on the propensity to misuse of buprenorphine *via* insufflation mirror the findings on intravenous administration. Several studies have reported substantial subjective rewarding effects from insufflated buprenorphine/naloxone, and there are no statistically significant differences with regard to actual intranasal self-administration between buprenorphine alone and buprenorphine/naloxone (29, 30).

Tolerance

Studies have shown no differences in safety or efficacy between the monotherapy product and combination formulation. However, it is not unusual for early clinical trials to overlook longer-term effects that may actually be harmful to patients. For example, one recent study comparing buprenorphine to buprenorphine/naloxone found no differences in mortality while patients were on treatment, but after treatment cessation mortality rates were significantly higher among patients who had been on the combination product (31). Preclinical studies have shown that prolonged exposure to even small amounts of μ antagonists such as naltrexone or naloxone can result in upregulation of μ receptors and a loss of tolerance for opioid-dependent individuals (32–35). These findings, in conjunction with a number of reported overdose deaths in the immediate aftermath of naltrexone treatment, have raised concerns that chronic use of opioid antagonists can predispose to fatal and non-fatal overdoses upon discontinuation of treatment (36). As noted above, oral administration of naloxone substantially reduces but does not eliminate its bioavailability. Naloxone is detectable in the urine of almost all patients taking sublingual naloxone/buprenorphine, with a median level of 60–70 ng/ml (37, 38). Tolerance to chronic opioids arises in part due to a shift in μ-opioid receptor effects from inhibitory to excitatory, and concentrations of naloxone considerably lower than 60 ng/ml are capable of reducing opioid tolerance by shifting intracellular coupling of μ-opioid receptors away from excitatory G_s proteins and back toward inhibitory $G_{i/o}$ proteins (39–42). If there were clear evidence that naloxone is effective at preventing misuse of buprenorphine, then an argument could be made that these potential risks are acceptable in light of proven benefits of combination therapy. Conversely, if naloxone does not act as a deterrent to parenteral administration of buprenorphine, then exposing patients to its potentially life-threatening side effects becomes harder to justify.

DISCUSSION

Based on the evidence outlined above, we cannot unambiguously conclude that naloxone is an effective deterrent to parenteral misuse of buprenorphine. At best, naloxone may reduce or delay the subjective "high" users experience, but in the absence of any dramatic effect on abuse liability, this partial blockade of subjective euphoric effects is of dubious clinical value. Epidemiologic studies have documented reductions in parenteral misuse of buprenorphine after introduction of the combination product, but some of this effect this may simply be due to patients hearing from their physician or from others in the medical community that naloxone prevents such misuse. It could be argued that, if it prevents a patient from ever attempting to take a buprenorphine/naloxone product parenterally, the message that naloxone blocks such misuse is of net benefit to the patient regardless of the actual pharmacological efficacy of naloxone in this regard. However, deliberately misleading patients is an ethical violation, even if we think it is in their best interest. This is one reason that, despite their many proven benefits, we do not actually prescribe placebos. The effectiveness of such interventions depends on trust that has been painstakingly cultivated over generations of interactions between the medical community and the public we serve. If information circulating in the recreational drug-using community is in reality more accurate than the information coming from the medical community, it can only be a matter of time before that hard-won trust is eroded. Our patients expect us to be honest and straightforward with them about the risks they face, and especially about the interventions, we recommend. The stakes are too high for us to do anything less.

AUTHOR CONTRIBUTIONS

CB contributed the conception and wrote the first draft of the manuscript; CB and JM wrote sections of the manuscript. All authors contributed to the article and approved the submitted version.

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The Opioid/Overdose Crisis as a Dialectics of Pain, Despair, and One-Sided Struggle

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The opioid/overdose crisis in the United States and Canada has claimed hundreds of thousands of lives and has become a major field for research and interventions. It has embroiled pharmaceutical companies in lawsuits and possible bankruptcy filings. Effective interventions and policies toward this and future drug-related outbreaks may be improved by understanding the sociostructural roots of this outbreak. Much of the literature on roots of the opioid/overdose outbreak focuses on (1) the actions of pharmaceutical companies in inappropriately promoting the use of prescription opioids; (2) "deaths of despair" based on the deindustrialization of much of rural and urban Canada and the United States, and on the related marginalization and demoralization of those facing lifetimes of joblessness or precarious employment in poorly paid, often dangerous work; and (3) increase in occupationally-induced pain and injuries in the population. All three of these roots of the crisis—pharmaceutical misconduct and unethical marketing practices, despair based on deindustrialization and increased occupational pain—can be traced back, in part, to what has been called the "one-sided class war" that became prominent in the 1970s, became institutionalized as neo-liberalism in and since the 1980s, and may now be beginning to be challenged. We describe this one-sided class war, and how processes it sparked enabled pharmaceutical corporations in their misconduct, nurtured individualistic ideologies that fed into despair and drug use, weakened institutions that created social support in communities, and reduced barriers against injuries and other occupational pain at workplaces by reducing unionization, weakening surviving unions, and weakening the enforcement of rules about workplace safety and health. We then briefly discuss the implications of this analysis for programs and policies to mitigate or reverse the opioid/overdose outbreak.

Keywords: opioids, overdose, despair, pain, one-sided class war, social conflict

THE OPIOIDS/OVERDOSE CRISIS AS A DIALECTICS OF PAIN, DESPAIR AND ONE-SIDED STRUGGLE

Millions of words have been written about the opioid/overdose epidemic in the United States, Canada and other countries (1–3). Many of the foremost experts on psychoactive drugs and the treatment of drug problems have written data-filled articles on the topic. So have many social scientists, pundits, and politicians.

This literature makes clear that the opioids/overdose crisis is multifaceted and complex (1, 2, 4). Understanding it takes transdisciplinary knowledge and transdisciplinary theory. In particular, knowledge about chemical dependency and drug treatment is too narrowly focused to come to grips with either the causes of the overdose outbreak or its solutions. Dasgupta, Belesky & Ciccarone provide a useful though general overview of the social and economic roots of the opioid crisis, including its relationships to "deaths of despair" based on changing economic conditions in some communities, and the interactions of these roots with other processes (5, 6). Jalal et al. after careful analysis of the contours of overdose rates in the United States since 1979, framed this as follows (2):

> This historical pattern of predictable growth for at least 38 years suggests that the current opioid epidemic may be a more recent manifestation of an ongoing longer-term process. .... Paradoxically, there has been substantial variability with which specific drugs have become dominant in varying populations and geographic locales. ....
>
> Understanding the forces that are holding multiple subepidemics together into a smooth exponential trajectory may be important in revealing the root causes of the epidemic.... Economic and technological "push" factors may be at work to increase supply, such as improved communications and supply chains, efficiencies in drug manufacturing, and expanding drug markets, leading to lower prices and higher drug purities (7, 8). Sociological and psychological "pull" forces may be operative to accelerate demand, such as despair, loss of purpose, and dissolution of communities (9, 10).

Their claim that overdose mortality has been increasing since 1979, that it has been based on a changing variety of drugs, and thus that it is likely the result of social or other processes of a general nature, seems to be accurate (11, 12). A National Academy of Sciences report made a related point (13):

> While increased opioid prescribing for chronic pain has been a vector of the opioid epidemic, researchers agree that such structural factors as lack of economic opportunity, poor working conditions, and eroded social capital in depressed communities, accompanied by hopelessness and despair, are root causes of the misuse of opioids and other substances and SUD.

Current efforts to address the opioid/overdose crisis have shown considerable imagination and involve the expenditure of additional funds for treatment of those whose lives have been disrupted by opioid use. Comparatively large amounts of research money are being devoted to this crisis. In particular, the Federal HEALing Communities initiative and other programs for rural communities and for criminal justice populations are devoting considerable money to learn how existing services and their coordination can be improved (14–17). It will be some years before we will know the extent to which these initiatives—which focus on only a small subset of the most impacted communities—actually improve current outcomes. It is important to note, however, that the thrust of these initiatives is to reduce harm to existing opioid users and to help some of them to stop using opioids. These are undoubtedly important goals. They are not the only goal, however. Although programs to reduce opioid prescribing may have some effect, and some community learning about the destruction opioid use can entail is undoubtedly taking place (and may be increased by these initiatives) (5, 18, 19), these programs themselves do not address the social roots of the crisis[1], and thus are unlikely to reduce the numbers of people beginning to use opioids or other potentially-fatal drugs greatly.

In this article, we first very briefly outline an overall model that ties upstream socioeconomic, political, and community forces to increases in opioid use. We then present an overview of data on the trajectory and magnitude of the epidemics of opioid use and fatal overdose. We then examine some of the proximal roots of this crisis— the role of the pharmaceutical industry and related changes in the funding and regulation of medical care, "communities of despair" (which is a term closely tied in with "deaths of despair') (3, 6), and *pain*, since the use of opioids in many cases is an attempt to alleviate physical and/or psychological pain, with special attention to the roots of such pain in various forms of alienation and in trends in the social nature of work and occupations. We then briefly discuss the implications of this analysis for action.

A BRIEF SOCIOHISTORICAL MODEL OF UPSTREAM PROCESSES AND PATHWAYS WHICH HELPED GENERATE THE OPIOID/OVERDOSE EPIDEMIC

Figure 1 presents an overview of this model. As has been well-documented, the period from 1947 through the early 1970's was one of relative labor-management truce and government focus on economic growth while respecting this peace in almost all industrialized countries (20–25). However, as discussed (and referenced) later in this paper, this truce was replaced by a period of one-sided class war in the 1970s that weakened unions, cut budgets for social services, reduced regulations in transportation (and other) industries in ways that weakened unions, and led to the victory of a political economy of neoliberalism and of ideologies emphasizing individualism and the right of companies to make profits over solidarity or mutual support. This led in the United States to a great growth in economic inequality, to economic recession and the development of the Rustbelt,

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[1] This is not a criticism of these programs. They are important and intelligent programs to determine how best to help people with opioid-related problems. That is a valuable goal—just not the focus of this paper. Likewise, we applaud and support the many grassroots and institutionally-based efforts to embed naloxone availability and use in communities to reduce overdose fatalities.

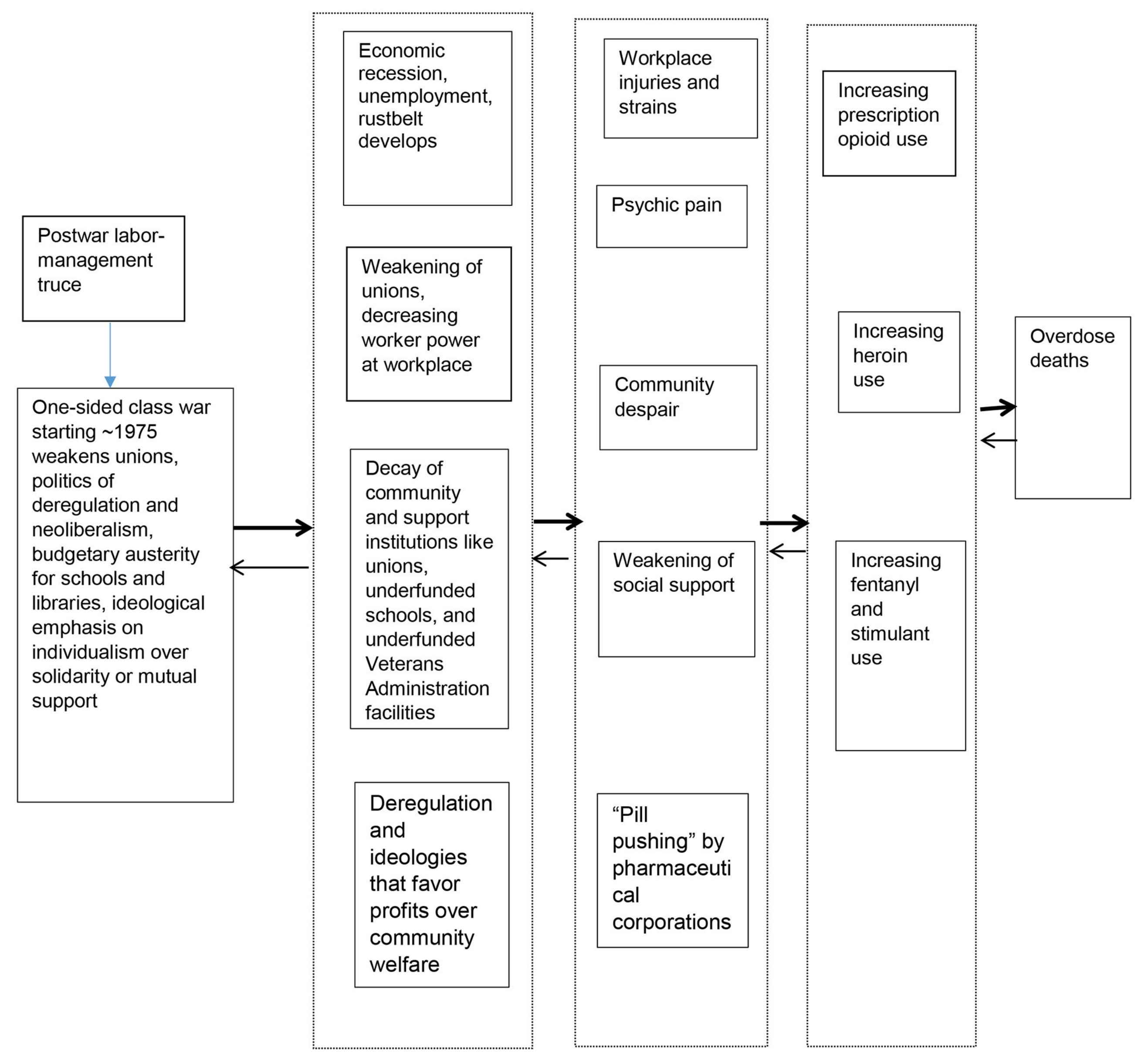

FIGURE 1 | A brief sociohistorical model of upstream processes and pathways through which they helped generate the opioid/overdose epidemic*. *As is discussed in the text, Items on the left seem to contribute causally to items to their right. A degree of reverse causation and of causal influence on items higher or lower in this diagram also seems to take place.

to weakened unions and reduced ability of workers to defend their working conditions, and to the decay of public schools and other community institutions. This set of events led to communities of despair and to workplace injuries—and thus to physical and psychic pain with reduced community capacity to offer social support to those suffering from these ills. Decreased regulation of pharmaceutical companies and the dominant ideology emphasizing the profitability of companies enabled and perhaps encouraged pharmaceutical companies to introduce new opioid products and to market them aggressively.

This set of processes paved the way for a great increase in prescription opioid use, followed by an increase in the use of heroin, and later of other opioids including fentanyl and of stimulants. Massive increases in overdose mortality were the result.

BRIEF REVIEW OF THE TRAJECTORY AND MAGNITUDE OF THE EPIDEMICS OF OPIOID USE AND OF FATAL OVERDOSE

The drug overdose epidemic has had multiple phases up to the current time (see **Figure 2**). While the number of drug overdose deaths has been increasing since 1979 (early in the one-sided

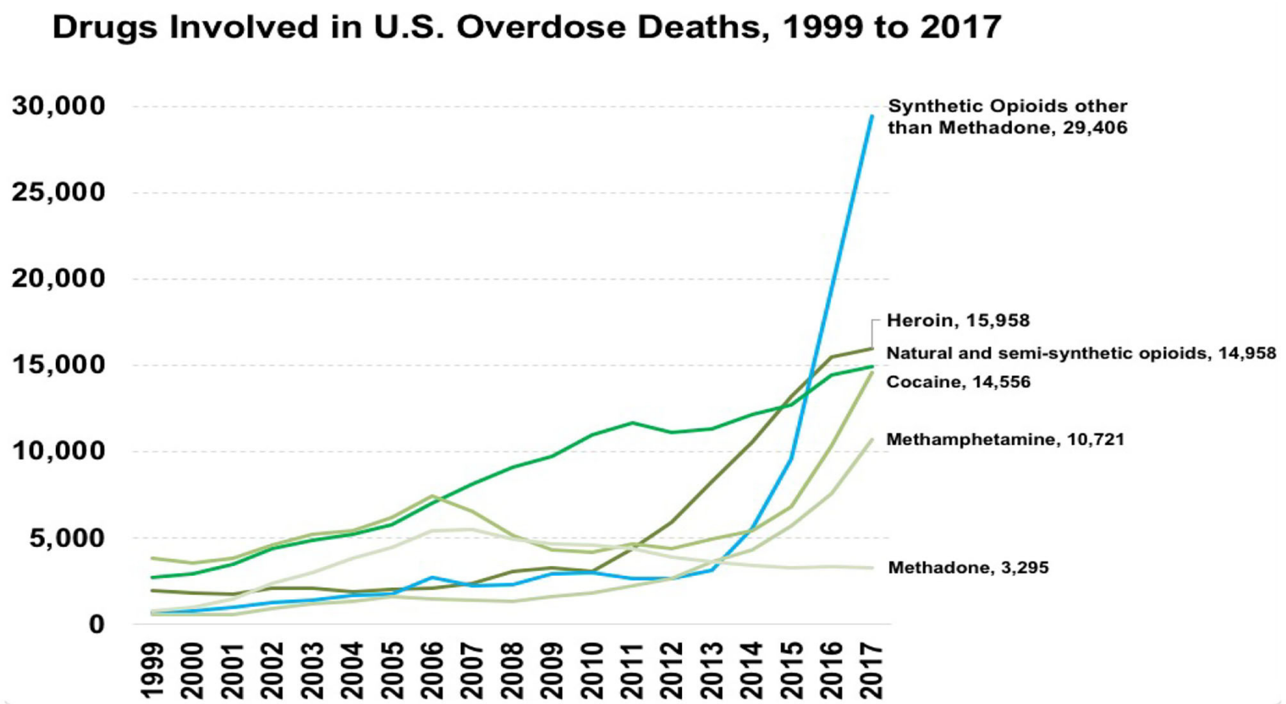

FIGURE 2 | Overdose deaths in the United States, 1999–2017. Source: Centers for Disease Control and Prevention (26)*. *All material in the MMWR series is in the public domain and may be used and reprinted without special permission; citation as to source, however, is appreciated.

class war), it entered a new period in the late 1990s when the first phase of the current epidemic period started with a rapid rise in the use of prescription opioids to treat chronic pain, a subsequent increase in prescription opioid misuse and in prescription opioid overdoses (27). The second phase started in the late 2000s when the prevalence of prescription opioid misuse and overdoses began to stabilize, but heroin use and heroin-related overdoses sharply increased. It has been hypothesized that the rise in heroin use is related to increased trafficking of purer and lower-priced heroin in the illicit market and to increased restrictions placed on the prescription opioid supply (28), with the Great Recession and its socioeconomic effects perhaps serving as a "Big Event" to exacerbate this increase and to produce an increase in methamphetamine use (29–32). A third phase began in 2013, with the introduction of illegally manufactured synthetic fentanyl and related synthetic drugs into the drug market. Overdose deaths spiked, as fentanyl and its analogs are considerably stronger than heroin, and are considerably stronger than heroin, and is often mixed in with other drugs, including other opioids, cocaine, and methamphetamine (33). It has been proposed that we are now in a fourth phase, characterized by polysubstance use, as overdoses involving both opioids and stimulants such as methamphetamine and cocaine have seen an increase, although this may be a continuation of trends in polysubstance use that began after the 2008 economic crisis (29, 34). It is not clear whether the three proximal partial causes of the overall epidemic that we focus on in this paper—pharmaceutical industry activities, community despair, and pain—were differentially important in these three phases, although it is likely that the pharmaceutical corporate contribution was greatest in the first phase.

Although death rates during this period of increased overdose mortality have been highest among American Indians and Non-Hispanic Whites, in recent years overdose mortality rates among African Americans and Hispanics have been increasing more rapidly (35).

THE ROLE OF THE PHARMACEUTICAL INDUSTRY AND RELATED CHANGES IN THE FUNDING AND REGULATION OF MEDICAL CARE

Much current thinking blames the early phases of the current opioid epidemic on the pharmaceutical industry and in some cases on inadequate regulation of this industry, coupled with an increasing push to consider pain as "the fifth vital sign" (36, 37). In 1996, the American Academy of Pain Medicine and the American Pain Society issued a consensus statement on "The Use of Opioids for the Treatment of Chronic Pain," which argued that opioids should have a role, even a first line role, in the treatment of patients with chronic non-cancer pain (38). Many states then enacted "Intractable Pain Acts" which removed sanctions for prescription of long-term and high-dose opioids. Opioid sales quadrupled between 2000 and 2010. As of 2017, 57 million people (17.4%) in the US received opioid prescriptions, including 15% of men and 20% of women (39).

The pharmaceutical industry played an important role in this push to consider opioids as a safe, non-addictive alternative to no treatment or to the use of other medications without addictive potential for chronic, non-cancer pain. The FDA approved OxyContin in 1996, which Purdue Pharma marketed as non-addictive and effective in treating chronic pain (40). The claim that OxyContin was non-addictive was based on one very flawed and small report (41); this statement is now considered to be factually incorrect (40, 42). The pharmaceutical industry spent tens of millions of dollars annually marketing prescription opioids to physicians, with a subsequent increase in opioid prescribing, including among physicians who received marketing-related payments from the pharmaceutical industry (43). Another important driver of prescription opioid proliferation was the creation of unregulated pain management clinics, or "pill mills," which functioned as hubs for distribution and sale of prescription opioids across the country (7, 44). For example, in Florida, where such clinics proliferated, and oxycodone-related overdose deaths increased 265% from 2003 to 2009 (8).

RESTRICTION OF THE PRESCRIPTION OPIOID SUPPLY AND THE RISE OF THE HEROIN MARKET

Federal and state governments responded to growing prescription opioid overdose deaths by regulating prescription opioids (e.g., approving supposedly abuse-deterrent formulations of oxycodone), controlling and monitoring legal access to prescription opioids (e.g., enacting regulations on pain clinics) and shaping prescribing practices (e.g., prescribing guidelines, prescription drug monitoring programs). Prescription opioid overdose deaths stabilized but heroin overdose deaths increased, perhaps because restrictions on the prescription opioid supply led to heroin use among people dependent on opioids (9, 10). (Prescription opioids and heroin have similar pharmacological properties, prescription opioids are often the first opioid used by heroin users, and people with a history of prescription opioid misuse are more likely to begin heroin use than non-users) (28, 45). For example, in one New York City sample of young opioid users, the average time from initiating opioid use to initiating heroin use was <4 years. However, the restricted prescription opioid supply was likely only one contributing factor to the rise in heroin overdose deaths. At the same time as prescription opioid became less available, heroin prices decreased and heroin purity and supply increased (42, 46, 47). After 2013, the introduction of fentanyl into the illegal drug market, and the adulteration of heroin with fentanyl contributed greatly to the rise in heroin overdose deaths.

COMMUNITIES OF DESPAIR

Another common explanation of the opioid crisis is that it is a reaction to economic and social despair, an argument usually tied to the decline in industrial manufacturing in most of the United States and the "rustbelt communities" it produced. This concept became popular through the works of Case and Deaton (3, 6) which described high death rates among US non-Hispanic whites, particularly among those with cumulative disadvantage and suggested that the prescription of opioids for chronic pain had exacerbated the problem (6).

Case & Deaton's work on this issue were widely publicized. The concepts of deaths of despair and communities of despair were further popularized by an article in *New York Magazine* by Andrew Sullivan (48). Recent evidence that the closing of automobile assembly plants may have increased opioid-related overdose mortality rates in their counties tends to support this argument (49). Relatedly, Pear et al. have shown that non-fatal overdose rates are more common in impoverished localities (50). Thomas et al. reviewed relevant qualitative research studies based in rural areas and found that economic, isolation and other physical conditions, social and policy environments were implicated in opioid-related harm (51).

It should be noted that despair leading to drug use is not a new concept—indeed the heroin and crack epidemics were largely concentrated in impoverished communities of color where lack of jobs, structural racism and over-policing and criminalization created despair in many people (19, 52–55). Opioid use continues to be high in many impoverished minority neighborhoods (56).

Sociological qualitative community studies help explain some of the processes through which changes in economic circumstances lead many people to opioid use or problematic drug or alcohol use (57–59). We will present evidence from two of these conducted in small New England cities. The first, Woonsocket, Rhode Island, is multiracial: In 2017, it was 64% White (60), 18% Hispanic, 6% Black, 7% Asian. The second, Weymouth, Massachusetts, is overwhelmingly (94%) White (61).

Ikeler's study of Woonsocket first provides a historical overview (58). It was a textile center for many years, and was 84% of its workforce was organized by the Congress of Industrial Unions (CIO) in the 1930s. The union established considerable control over workplace life, and over the culture and daily life of the community.

Starting in the 1950s, however, an early Rustbelt experience came to Woonsocket as textile companies moved their production to the US South. A large proportion of Woonsocket's workers, and their descendants, found employment only in short term, precarious work for temp agencies or retail shops. As Ikeler argues:

> Attachment to the formal economy or even to a craft or occupation that could provide "ontological security" had declined considerably in post-industrial Woonsocket. . . .
> Yet when work is no longer dependable and its forms increasingly vary—customer service, construction, cab driving, you name it—it ceases to be a dependable site for effort expenditure and identity formation. Precarious workers find alternatives.

These alternatives often involve alcoholism and drug use. As Ikeler goes on to describe:

> Alongside fragmented work and absent union experience, subjects described, over and over, the continuity and immanence of substances. Many were not themselves addicts but all witnessed heavy, endemic use in their immediate surroundings.
>
> .... Substance use appeared to replace work as the most unifying daily practice; resisting it appeared to replace unionism.

Many of the participants in Ikeler's research both used opioids and other substances and continued to work at those precarious jobs that were available to them. They also fulfilled family roles such as mother and father. In many cases, they did these roles well. Thus, as one participant reported:

> "My parents are both junkies," she told me. "They were good parents though, always emotionally there, just addiction gets annoying." Corinne had dabbled in opioids herself: "I did heroin only a handful of times and I was like 'this is stupid' so I stopped." But she opined on the reasons for its use around her: "I think it's a hard time," she said, referring to the economy. "And it's easy—people get depressed, it's easy to grab a bottle or do heroin and just not think for a little awhile. That is why I did it."

Ikeler goes on to present a complex picture of contradictory tendencies in Woonsocket's community culture. On the one hand, there are forces which lead many people to take up substance use. On the other, neighbors support each other when someone has problems due to drug use and/or when people attempt to quit using drugs.

Ikeler summarizes his analysis as follows:

> These stories suggest two things. First, they display the depth and pervasiveness of substance abuse in general and opioid abuse in particular among key groups of contemporary workers. They show this in a way that is not simply parallel to other pursuits, such as work, family, or hobbies, but central and in many ways a replacement.
>
> But second, ... they display a reorientation of resistance toward their own habits and those of users around them. Either way, this struggle is internal: internal to the *self* among recovering addicts; internal to *working-class communities* among nonusers.
>
> Class-based resistance ...has thus not entirely disappeared in the 21st century. It has in large part been redirected toward substances, the new agents of dependence, rather than employers.

He then briefly discusses the contradictory experiences of West Virginia. He presents data showing that West Virginia had the highest rate of overdose deaths of any state in 2016 and that it had seen the fifth highest decline in union density from 1983-—2016. In spite of this (or perhaps in part as a consequence of this), West Virginia was also the state where the mass teacher strikes of 2018 began, and where they got massive community support, undoubtedly including support from many people who use opioid and their families and neighbors.

Susan Starr Sered conducted an ethnographic sociological study of Weymouth, Massachusetts, a suburban blue collar town south of Boston (57). Her overall analysis complements Ikeler's, in part because she focused less on the experiences of people using drugs and more on issues of what she calls social and cultural capital as described by a wide range of community residents. Like Ikeler, she describes the decline of union employment as leading men (particularly) and women to lose access to long-term full time employment. Unlike Ikeler, and relevant to our discussion of how one-sided class war facilitates both occupational pain and community despair–and thus opioid use, she reports that:

> A long-time union member explained, "In working class communities people get injured on the job [and then are] overprescribed pills. If they don't go to work they don't get paid so they fight through injuries. And then one thing leads to the next and the next."
>
> Although occupational injuries and subsequent use of pain medication made pills accessible, Weymouth residents more often related the current opioid crisis to the "lack of hope for decent [blue collar] jobs," especially for young men. Thus, several respondents talked about teenagers getting their start with drug mis/use with "finding" pain pills in the medicine cabinets of their blue collar parents. In other words, the parent may have used and perhaps misused prescription pain medication but for the most part in ways that did not significantly interfere with managing a job and daily life. But the kids ... took their drug use up to a whole new level.
>
> Like Ikeler, she also shows ways in which the dominance of precarious employment generates a crisis of meaning and of identity. She describes this in terms of "cultural capital; that is, the repertoire of meaningful scripts that help individuals and communities make sense of life's pain, challenges and tedium. Without meaningful scripts, individuals and communities may be more inclined to misuse mind and mood altering substances in order to manage their pain, disappointments and restlessness." Major sources of decline in such cultural scripts that she identifies include changes in the local school system from one that helped blue collar children form social ties to one oriented to college-based careers focusing on individual material success and problems caused by neoliberal attacks on other public institutions like the Veterans Administration.

She then added:

> As access to varied useful and healthy ways to interpret and manage suffering declines or is blocked, opioids and other pain killing and mood changing substances may come to be seen as the only or the most available means of dealing with pain of all kinds.

PAIN: TRENDS, AND ITS SOCIAL ROOTS

As Sered mentioned, a third proximal cause that has been pointed to for increases in opioid use and overdose deaths is pain, both physical and psychic (57). As discussed above, although pharmaceutical companies increased the supply of opioid pain relievers and engaged in aggressive marketing of these products, initial uptake of these medicines depends, at least in part, on the extent to which people being offered or asking for prescribed opioids, as well as potential prescribers, feel that pain relief would help them. (We specify "initial uptake" because opioid dependence or enjoyment can change the motivations for use).

As we discuss below, there is considerable, though contested, evidence than pain has been increasing in the United States.

Supporting such a claim, however, is difficult, because data on pain have many sources of inaccuracy. One potential source of inaccuracy is that to the extent that data depend on self-reported or self-assessed pain levels, there are possibilities both for culturally-induced biases to enter the data, for public attention to pain to increase perceived need for pain relief, and for differential responses by respondents who use different metrics for assessing their own pain levels. In addition, as Dasgupta et al. argue, people sometimes somaticize economic hardship and other stresses into the form of pain, and this could affect both the statistics and the extent of pain suffered by the population (1).

The United States Institute of Medicine considered these issues in a report issued in 2011 (62). It concluded that approximately 100 million Americans suffered from chronic pain. Basing itself in part upon NHANES data, it found that pain had been increasing in the United States. More recently, Nahin et al. used data from the Medical Expenditure Panel Survey to show that non-cancer-related pain that interfered with daily work (including both work outside the home and work in the home) had increased from 1997/98 to 2013/14 among US adults (63). Overall, the proportion of adults reporting painful health condition(s) increased from 32.9% (120 million adults) in 1997/1998 to 41.0% (178 million adults) in 2013/2014. The use of what they classified as *strong* opioids increased more than did non-cancer pain, as did the use of strong opioids within each level of pain interference with work. This trend was particularly strong among those with severe interference due to pain, where the use of strong opioids increased from 11.5% (4.1 million adults) to 24.3% (10.5 million adults) (2).

Nahin et al. also summarize some of the specific causes of pain that have been increasing. These include musculoskeletal conditions, particularly arthritis and spine-related outcomes, and also mental disorders. Keyes et al. point out that both non-medical opioid use and chronic pain and injury are more common in rural areas (64).

Workplace Sources of Pain

Our model of upstream processes suggests that the one-sided class war leads to less worker control, or even input into, working conditions, safety, and ability to socialize on the job, and thus to loneliness and despair, all of which can lead to more physical and psychic pain (1). The study of what happens at *workplaces* is an issue that many economists, drug researchers, and epidemiologists rarely study (13), even though some earlier reports on increasing opioid deaths dealt with workers' compensation data (65). For example, as shown in the quotation in the Introduction to this paper, the NAS report on *Pain management and the opioid epidemic* mentioned working conditions, but did not substantively examine them. In their otherwise insightful review of the opioid crisis, Dasgupta, Beletsky & Ciccarone do mention working conditions and their association with pain, but do so primarily in connection with poverty and with conditions in poor communities (1). They do not explore the mechanisms or time-trends that might contribute to workplace issues causing *increasing* substance use or overdoses by causing pain. A recent overview show the evidence for and importance of workplace environments in causing physical and psychological pain, opioid use and overdose deaths, but does not tie this into changes in union power and efficacy or to the economic and social changes tied to the one-sided class war (66).

Leukefeld et al. (p. 516) discuss how medicating pain with pain killers had become a part of the culture in Appalachian Kentucky based on the needs of loggers and miners who suffered from occupationally-related pain (67). Specifically, they report that:

> Overall, these seventy key informants agreed with the media that the non-medical use and misuse of prescription drugs is widespread and has been a long standing problem with "deep roots" in Appalachian Kentucky and could be part of the "culture." …This rural drug culture was described by our key informants and others as emerging from loggers who worked with limited power equipment and coal miners who worked bent over in three to four foot high coal mines. The families of loggers and in "coal camp communities" accepted the use of prescription drugs to relieve physical pain and to help wives cope with their depression and their "depressing" surroundings

Buer's *Rx Appalachia* provides additional data about how occupational injuries and Black Lung had led to opioid use, to stressful family situations, and thus to opioid use by family members of those suffering from workplace-induced pain (68, 69).

Cross-sectional data show that people who work in industries and occupations in which workplace injuries or other sources of pain are prevalent are more likely to die of drug-related overdose. *MMWR* reported this for national data for 2007–2012, finding that "Construction occupations had the highest PMRs [proportional mortality ratios] for drug overdose deaths and for both heroin-related and prescription opioid–related overdose deaths. The occupation groups with the highest PMRs from methadone, natural and semisynthetic opioids, and synthetic opioids other than methadone were construction, extraction (e.g., mining, oil and gas extraction), and health care practitioners" (70). A detailed report from Massachusetts for later years (2012−2015) found similarly that construction and extraction occupations were at highest risk; specified that those in health care who were at high risk were health care support staff; and added that those in farming, fishing, and hunting; material moving; installation, maintenance and repair; transportation; production; food preparation and related positions; and building and grounds cleaning and maintenance were also at enhanced risk (71). Cerdá et al. found that, in California, localities with more manual labor industries had a higher rate of hospital discharges for prescription opioid poisoning (72). Most of the industries mentioned above are occupations in which musculoskeletal injuries are frequent. Some of them are also among the occupations in which employment has been growing rapidly; and in these and other industries, the effects of the one-sided class war discussed in depth below also tend to produce more injuries and more physical and psychic pain.

Ompad et al. used National Survey on Drug Use and Health data to compare drug use among construction and extraction workers to that among other workers (73). They found that construction and extraction workers were significantly more likely to report non-prescription opioid use. Missing work due to sickness or injury was also associated with non-prescription opioid use.

"ONE-SIDED CLASS WAR"

We have discussed three major facilitators of the opioids/overdose crisis: actions by pharmaceutical companies, the growth of communities of despair, and increased pain among the population, particularly that owing to injuries, exposures or other sources of pain at work. None of these processes is easy to reverse, although court cases and opioid regulation may have some effect on pharmaceutical industry actions. This suggests it might be useful to investigate whether these three processes have common sources that might be changeable.

Many commentators have investigated these issues. In general, they point to economic globalization, the growth of neoliberal policies and ideologies that include restricting regulation of corporations' activities (including both regulation of pharmaceutical companies and oversight of employers' actions that might lead to injury or harmful exposures of their employees) and result in the movement of much manufacturing and other economic activity away from the Rust Belt. They generally see economic globalization as enforcing a mode of competition that works symbiotically with neoliberalism to create a "race to the bottom" for social welfare and labor protections (24, 25, 74). In some cases, they see these changes as irreversible—which would imply that these drivers of the opioid/overdose crisis might also be irreversible.

The framework we presented at the beginning of this paper and in **Figure 1** presents a more hopeful perspective. It frames changes such as globalization, deregulation, and neoliberalism as part of a process of "one-sided class war" through which corporate interests and their political supporters have enforced the dominance of corporate profitability, neoliberal ideology, a global pattern of commodity chains in which production is done where it is cheapest (which forces workers and localities to compete with the poorest countries for employment), and the financial "bottom line" over government policies all over the world. This effort has succeeded in creating declines in unionization, social welfare, protective regulation, and labor standards, and has led to pressures to convert education and health care into profit-making enterprises (75). This one-sided class war framework has been presented in books by Harvey, Davis, and Moody, among others (20–22, 24, 76, 77). The basic thrust of this position is that in the mid- to late-1970s, those who own and run large businesses switched to a more aggressive stance toward unions, social programs, and regulation of business.

One of the first examples of this successful one-sided class war campaign was the "New York fiscal crisis" of 1975 where financial institutions declared that the debts of New York City required massive cutbacks[2]. After New York State established a fiscal control board in charge of the City budget, it made major cuts in municipal services and spending, froze municipal salaries (at a time of rapid increases in the cost of living), laid off large numbers of civil servants, including many union members, raised bus and subway fairs, cut welfare spending, and closed many local hospitals, libraries and fire stations. They also successfully demanded that the unions representing city workers allocate much of their pension funds to the purchase of city bonds—putting the pensions at risk if City bankruptcy took place. As Wallace & Wallace have shown, the closures of fire stations and the general onset of austerity led to massive fires breaking out and spreading in the poorer, mainly Black and Latino, areas of New York (78). These, in turn, led to extreme overcrowding in nearby areas as the dispossessed sought places to live, the decay of school and recreation facilities for youth, and an increase in drug use and vulnerability to infectious disease epidemics such as of tuberculosis and HIV (79).

The one-sided class war took many forms. One of these was the deregulation of the air and trucking industries, which greatly weakened union power and protections for workers in these large industries. More broadly, business increasingly took anti-worker and anti-welfare stands on a wide variety of legislative and administrative issues. This led to some militant rhetoric by some labor union leaders and others—rhetoric which was not by and large backed up by their later actions. A symbolic example of this was a letter made by Doug Fraser, President of the United Automobile Workers, which was at that time a powerful union if and when it chose to strike. This event is described in an article by Jefferson Cowie as follows (75):

> In July of 1978, Douglas Fraser … resigned from John Dunlop's Labor-Management Group in a flurry of publicity. The committee had been set up under the Nixon administration to seek out cooperative solutions to labor-management problems and to pass advice along to the White House. Although the group was supposed to reflect the postwar consensus in labor-management relations, Fraser's public resignation and the press conference that accompanied it shredded the fiction of that consensus …. "I believe leaders of the business community, with few exceptions, have chosen to wage a one-sided class war today in this country- a war against working people, the unemployed, the poor, the minorities, the very young and the very old, and even many in the middle class of our society," he declared. "The leaders of industry, commerce and finance in the United States have broken and discarded the fragile, unwritten compact previously existing during a past period of growth and progress."

Later, as Cowie describes, the letter argues that:

> The new flexing of business muscle can be seen in many other areas. The rise of multinational corporations that know neither patriotism nor morality but only self-interest, has made accountability almost non-existent. At virtually every level, I discern a demand by business for docile government and unrestrained corporate individualism. Where industry once yearned for subservient unions, it now wants no unions at all.

As we discussed above, the increase in overdose deaths began in 1979 and has increased dramatically since then (see Footnote 2). During this time, the dominance of neoliberal ideology and

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[2] This is an example of a Structural Adjustment Program being applied to a major city in a core superpower.

globalization of investment and supply chains proceeded apace, as did the decline in unionized percentages of the workforce. (And as discussed above, Ikeler has presented evidence that the decline of unionization has been a predictor of overdose deaths both longitudinally and cross-sectionally) (58). Elections in both the United States (Reagan) and the United Kingdom (Thatcher) put explicit advocates of neoliberal ideology and policies in charge of two major countries. The Federal Reserve of the United States soon thereafter enacted policies designed to "contract" the economy and thus to increase unemployment—which often meant that companies moved industrial production out of what became the Rust Belt to areas where unions were less prevalent so lower wages could be paid and working conditions worsened in efforts to improve productivity rates.

In both the US and the UK, nationally-coordinated efforts deliberately provoked powerful unions to strike and then mobilized the power of the government and of corporate-owned media to defeat the strikes and (in the US) to de-certify the union (the Professional Air Traffic Controllers Organization). Large-scale decreases in the staffing and the authority of regulatory agencies have also taken place. The power of US unions, and the ability of workers to resist worsening work conditions, has been weakened by bureaucratic internal union regimes; racial/ethnic divisions; political dependence on the Democratic Party; the lingering effects of the red-baiting era and other factors (22, 80–82).

The Great Recession that began in 2007 exacerbated many of these effects by increasing fiscal pressure on governments to implement austerity programs and by increasing unemployment, part-time employment and precarious employment—which have been associated with increased injury rates and other sources of pain—and it should be noted that sharp increases in overdose deaths from opioids and stimulants began shortly thereafter (83).

Pharmaceutical companies were assisted in become massive purveyors of addictive pain medicines by the reduction of government regulatory power over corporations and by the dominance of neoliberal ideologies that support companies' taking actions that yield large profits without regard to "collateral damage". This was also facilitated by active intervention on the part of pharmaceutical companies to influence clinical pain treatment assessments, guidelines and practices (1). Furthermore, since the era of neoliberalism has been a time in which short-term gains have been emphasized as the key economic indicator, corporate managers and boards of directors were induced to strive for high profits even if some patients might become opioid-dependent as a result. Finally, another thrust of neoliberal thought, and one which has been useful in helping corporations take potentially-profitable activities away from state control, has been the emphasis on *efficiency via cost-cutting* (84). In health care systems, this has taken the form of insurance companies' decisions that doctors and medical organizations can only be reimbursed for performing particular activities, and the pressure this creates for medical institutions to emphasize that doctors process patients rapidly. One aspect of this process was a de-emphasis on behavioral pain therapy and an emphasis on using pharmacotherapy, i.e., analgesics—and particularly opioids—as a way to treat pain (1). In sum, then, the one-sided class war impelled pharmaceutical corporations to maximize their profits lest they go bankrupt or face hostile take-overs, made the production and aggressive marketing of opioid a lucrative way to do this, and reduced regulatory and other counter-pressures that might have deterred them from emphasizing opioids.

The one-sided class war also created communities of despair. Our discussion above showed how it led to the economic abandonment of many communities by manufacturing and other industries that had previously provided stable jobs (with health and other stabilizing benefits); to the destruction or significant weakening of unions that provided social support and identity to many residents; and to the weakening of schools, youth programs, and other community institutions (57, 85, 86). In addition, the neoliberal project that has been a major political form that one-sided class war took has included an ideological emphasis on "individual responsibility" and thus on "individual blame" for failure. Political leaders of both parties, notably including both Presidents Reagan and Clinton, emphasized personal responsibility and the guilt of failure. Thus, neoliberal ideology frames the effects of economic disasters and social institutional decay on each individual and on each family member as being their own fault. This sense of failure, guilt and hopelessness is a major component of communities of despair. Scripts and solidarities that can oppose this sense of guilt and failure were, as both Ikeler and Shered Starr demonstrate, greatly weakened as their institutional bases like unions and some public school systems were attacked by the powerful and as over-policing interacted with these to create a "school-to-prison pipeline" and neighborhood disruption (87). Further, as these same authors also demonstrate, opioids and other psychoactive substances have helped to alleviate (albeit perhaps transiently and with later resultant morbidity) the psychic pain, and drug cultures have created some oases of solidarity.

The discussion above showed that there are positive associations of high-risk occupation and industry with drug use and with fatal overdose. Moody's work, among others, describes pathways through which one-sided class war contributed to increases in both acute and chronic pain. One historic function of unions has been to protect the health and safety of workers. When unions have been stronger, this has been more effective; when they have been weaker, injuries and painful exposures have increased (21, 22, 88–90). Similarly, the ability of individual workers and work groups to defend their safety and health is stronger when their economic security is greater and when solidarity-supporting belief systems are stronger in a community. In the absence of these protections, employers force workers to work more; workers are less likely to hear of and respond to dangerous machinery or risky occupational exposures in time to prevent adverse consequences; and workers are less able to help each other resist management demands that they perform tasks that might lead to musculoskeletal or other injuries. Similarly, many of the employed and some classified as "unemployed" work at part-time or off-the-books jobs with even less than average protection against injury and pain. This is one reason why overdoses are high in agricultural, restaurant and non-union sectors of construction work.

In addition, the lack of worker power on the job often leads to, and perhaps results from, workers' having no time to be sociable or form bonds of solidarity on the job. Further, employers control work-time scheduling so that workers' schedules do not overlap as much as in traditional work. This can contribute to loneliness and to demoralization both at work and in the community—and this, in turn, can open paths to drug use.

Another way in which one-sided class war can lead to higher rates of painful exposures and injuries is through deregulation. Protective government organizations like the Occupational Safety and Health Administration (OSHA) have had their authority to conduct workplace inspections reduced. They have also been starved budgetarily, which has resulted in great reductions in staff availability to conduct inspections. (Similar pressures have also weakened the statistical ability of the government to produce accurate and consistent records of workplace safety and health).

In sum, then, one-sided class war has been a major contributor to the opioid/overdose epidemic by facilitating pharmaceutical companies in their push to increase profits through selling addictive pain medications, specifically opioids; creating communities of despair; and contributing to pain in the population. This suggests that ending (or at least reducing) the one-sided class war might help address the opioid/overdose epidemic.

INTERNATIONAL OPIOID EPIDEMICS: EVOLVING EVENTS AND CONSIDERATIONS

The discussion and analysis above have focused on the United States, which has been the country most dramatically affected by the opioid epidemic. However, a very similar constellation of forces has led to a significant opioid epidemic in Canada (91–94), affecting every region of the country, albeit unevenly as has occurred in the US. Given that the processes of neoliberalization which contributed to the environment in which the opioid epidemic developed in the US and Canada have also impacted many other countries, reasons for the lack of apparent development of opioid epidemics elsewhere require further study. One potential factor contributing to the varying risk of opioid epidemics in different countries may be the nature of their respective health care systems; health care systems which are primarily for profit and without a single payer, and where high proportions of the population lack health insurance (as in the USA although not Canada) may be at greater risk for a variety of reasons, including that these factors may make if more profitable for pharmaceutical companies to heavily market opioids. Use of restrictive national formularies, which limit the types of opioids which may be used for non-cancer pain, and more restrictive prescribing regulations, may also play a role (95). A study comparing opioid prescribing in eight countries, for example, found that US patients were more likely to receive opioid prescriptions than patients in other countries (96). There are also differences in national and regional regulations which limit various forms of advertising and marketing as well as degrees to which pain treatment guidelines were influenced by pharmaceutical companies. Nonetheless, it is also plausible that opioid and overdose epidemics may occur at different times in different countries due to different balances of "market forces" (meaning neoliberalization, de-industrialization, occupational pain), pharmaceutical marketing efforts and class struggle. Importantly, there are reports that pharmaceutical companies are currently utilizing marketing strategies (such as claims of low addictive potential) that have been curtailed or diminished in the US and Canada, in other countries such as Germany, Italy, Australia, Brazil, Mexico, China and elsewhere (97–99). Also, opioid consumption is increasing in the Netherlands, and the UK NHS has reported that the number of opioid prescriptions has risen dramatically from 2008 to 2018 (100, 101).

There are, of course, many other forces and processes that affect which drugs are available for sale in which locations around a given country or the world. For example, the presence of synthetic fentanyl as a street drug or laced in the heroin drug supply has been reported much more frequently in U.S. relative to most European counties, and likely contributes to differential opioid use and overdose patterns across these regions (102).

Finally, there are clear differences in the extent to which the class war has been one-sided in different countries of the world (22, 77). The United States has long been an outlier among developed countries for lacking a large socialist, social democratic, labor or communist party, for example. In addition, at the start of the period of one-sided class war in the United States, the labor movements in different countries varied widely in political power, organization and capacity to disrupt the economy. The United Kingdom, for example, had a very strong shop stewards movement that was able to organize widespread strikes that drove at least one Prime Minister from power, whereas no comparable capacity existed in the United States. Although the period since then has seen many defeats for workers in Britain, they retain both influence in the Labor Party and capacity for strike action that, at least until 2016, are far greater than comparable forces in the United States. Research is needed on the extent to which these differences underlie international differences in the degrees of regulation imposed on pharmaceutical opioids, the extent of occupationally-induced pain, and/orthe dynamics of communities of despair or the ways in which members of these communities do or do not get involved in opioid use.

More research on the international dimensions and implications of the opioid and overdose epidemics are clearly needed. The discussion in this section suggests that such research will need to consider a wide range of social, economic, political and regulatory factors and will need to consider both the historical records and longitudinal data.

IMPLICATIONS FOR ACTION

Many strategies have been proposed and some implemented for dealing with the opioid/overdose crisis. The Federal and some state governments have expanded drug treatment availability, including evidence-based medications for opioid use disorder.

This is much needed; treatment gaps in the United States are huge (103). Efforts are being made to improve coordination among treatment, harm reduction, law enforcement and other community organizations, and to increase availability of naloxone with which to conduct overdose reversals. In addition, the medical community is shifting standards for pain prescribing, and both regulation and law suits have served to reduce pharmaceutical corporations' efforts to increase prescription opioid use. It is too soon to tell whether these efforts will reduce the overdose crisis. It is notable that overdose mortality due to stimulant use has been increasing rapidly in recent years. Furthermore, harm reduction and drug treatment services, as well as drug treatment regulations, budgets, and the cultures of many communities (and of people who use drugs within these communities) have been deeply affected by the COVID-19 pandemic and its related socioeconomic crises, with unknown implications for the future of opioid and stimulant use and of overdose mortality (104–106).

Harm reduction efforts such as expansion of naloxone access, as well as efforts to regulate opioid prescribing through prescription drug monitoring programs and pain management clinic laws, have been associated with reductions in opioid overdose deaths (107–112). Indeed, following investment in multiple efforts to curb high risk prescribing and regulate overall opioid prescribing, prescription opioid overdose rates leveled off (although they did not decrease). At the same time, overdoses involving synthetic opioids continue to increase, as well as overdoses involving both opioids and stimulants.

Furthermore, there is a strong likelihood that in the absence of action to reverse the one-sided class war, conditions in American communities will get worse for a majority of people due to further cuts in services, further rollbacks of safety regulations, and the increasing consequences of climate change and its many ramifications (113, 114). The worsening conditions are likely to increase despair and to produce additional sources of injury and pain. Thus, unless the disruption due to climate change disrupts access to drugs, these changes are likely to induce additional drug use and overdose mortality.

The COVID-19 pandemic and its associated economic crisis may have devastating impacts on efforts to reduce community despair and occupational pain. These events have created enormous costs for state and local governments and have reduced their revenues to a great degree. Political battles over how to make their budgets are likely to occur as long as the economic crisis persists, and to be full of conflict. The one-sided class war has created the conditions under which what Naomi Klein has called the "Shock Doctrine" is likely to be successful (115). The Shock Doctrine describes how corporations and politicians use crises to seize the initiative and cut public services such as schools, welfare and public health and eliminate regulations that limit what corporations can do. These are precisely the types of policies that have facilitated the opioid/overdose crisis. Beyond that, such policies are likely to lead to cuts in treatment for opioid use disorder and other drug treatment approaches, and perhaps weaken harm reduction programs as well.

The analysis in this paper points to counteracting the one-sided class war as a strategy that focuses on an upstream cause of pain, community despair, and pharmaceutical sales of addictive medicines, and that also organizes power to resist Shock Doctrine kinds of attacks. (We would argue that this would have many advantages to many people in addition to those specifically concerned with drug use and overdose, including making it more feasible to reduce greenhouse gas emissions. Those who support or profit from the one-sided class war might disagree).

Counteracting the one-sided class war is not easy, and will involve internal discussion and struggle within the working class among racial/ethnic groups, gender groups and among people with different employment statuses and occupations. These issues have been discussed by scholars and activists from many disciplines (22, 77, 80, 82, 116, 117). We will not propose a fully developed strategy for addressing these issues here. The social and economic disruptions related to COVID-19 have created a rapidly changing sociopolitical and economic environment that poses particular difficulties for strategic planning at this time, although they also offer opportunities for social change (see below).

> What we will do is point to two general lines for strategic action. These should be studied and evaluated.

The one-sided class war has been supported politically by the ideologies of neoliberalism that posit individuals and corporations as the building blocks of society and see governments (except in their law enforcement and military mores) as taxing away resources from these building blocks and as limiting individuals' and corporations' freedom to innovate and bring prosperity. One strategy for weakening or reversing the one-sided class war is to attack these ideologies. Indeed, many people have been trying to do this since the 1970s. Articles like this one, which show some of the harmful effects of neoliberal one-sided class war, are indeed inherently part of this strategy.

The other basic strategy is to make the class war two-sided. In recent years, but before COVID-19, mass teacher strikes that had won gains for teachers, other government employees, and school kids had shown that such an approach can make gains. Events during the first half of 2020 have initiated a period of social contestation that seems to create additional avenues for opening up the class war insofar as they have led to mass activism by Black people and their allies around police violence and other issues. It should be remembered that similar movements in the 1960s contributed to increases in both union organizing and active struggle within and by previously organized unions (including struggles over racism within unions) (80, 81, 88). The first half of 2020 has also seen a wave of more wildcat (unofficial) and other strikes than have taken place for decades (118). Mass struggles over how to resolve the COVID-19-related budget deficits in state and local governments are just one form of such likely struggles over the next few years. More generally, efforts to build a mass-based social movement unionism along the lines Moody has put forward, if successful, could do much to make the class war two-sided and to reduce community despair and occupational pain and injury (22).

Community organizing of various sorts can also help blunt and reverse the damages wrought by one-sided class war. Indeed, Moody, Shered Starr and Ikeler all point to ways this can be done. We would add, based on our experience and that of harm reductionists globally, that people who use drugs have set up organizations of their own in some areas that sometimes take part in community and other activist movements. They can be effective members of such community organizing, and can contribute to ensuring that community and union efforts address opioid- and overdose-related workplace and community problems.

In sum, then, one-sided class war has been an important upstream contributor to the chain of causation that has led to, and continues to drive, the opioid and overdose epidemics. Our paper points to important issues for new research to address and to new intervention approaches that might help reduce opioid and overdose problems.

AUTHOR CONTRIBUTIONS

SF took overall responsibility for the paper. MC drafted some sections. All authors contributed ideas and contributed to the writing of the paper, and reviewed it and agreed it should be submitted.

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Breaching Trust: A Qualitative Study of Healthcare Experiences of People Who Use Drugs in a Rural Setting

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Background: Increased drug use has disproportionately impacted rural areas across the U.S. People who use drugs are at risk of overdose and other medical complications, including infectious diseases. Understanding barriers to healthcare access for this often stigmatized population is key to reducing morbidity and mortality, particularly in rural settings where resources may be limited.

Methods: We conducted 20 semi-structured interviews with people who use drugs, including 17 who inject drugs, in rural southern Illinois between June 2018 and February 2019. Interviews were analyzed using a modified grounded theory approach where themes are coded and organized as they emerge from the data.

Results: Participants reported breaches of trust by healthcare providers, often involving law enforcement and Emergency Medical Services, that dissuaded them from accessing medical care. Participants described experiences of mistreatment in emergency departments, with one account of forced catheterization. They further recounted disclosures of protected health information by healthcare providers, including communicating drug test results to law enforcement and sharing details of counseling sessions with community members without consent. Participants also described a hesitancy common among people who use drugs to call emergency medical services for an overdose due to fear of arrest.

Conclusion: Breaches of trust by healthcare providers in rural communities discouraged people who use drugs from accessing medical care until absolutely necessary, if at all. These experiences may worsen healthcare outcomes and further stigmatize this marginalized community. Structural changes including reforming and clarifying law enforcement's role in Emergency Departments as well as instituting diversion policies during arrests may help rebuild trust in these communities. Other possible areas for intervention include stigma training and harm reduction education for emergency medicine providers, as well as developing and implementing referral systems between Emergency Departments and local harm reduction providers and medically assisted drug treatment programs.

Keywords: rural, opioid, inject, drugs, healthcare, stigma, access, barriers

INTRODUCTION

People who use drugs, especially via injection, are at increased risk for medical complications, including HIV, hepatitis C virus (HCV), sexually transmitted infections (STIs), endocarditis, skin and soft tissue infections, psychiatric illnesses, and overdose (O'Connor et al., 2014; Kievlan et al., 2015; CDC, 2018, 2019). It is also highly likely that people who use drugs are at increased medical risks from COVID-19 (Vasylyeva et al., 2020; Volkow, 2020). Despite these risks, people who use drugs access primary care less often and utilize emergency medical services (EMS) more frequently than the general population. The under-utilization of preventative healthcare services in this population can lead to a variety of adverse health outcomes, including high infectious disease prevalence and poorer mental health, as well as higher costs from medical complications and overuse of EMS (French et al., 2000; Ahern et al., 2007; Patrick et al., 2012; Artenie et al., 2015; Paquette et al., 2018; von Hippel et al., 2018).

One explanation for the under-utilization of medical care by people who use drugs may be their experiences with stigmatization. (Earnshaw and Chaudoir, 2009) conceptualized the theory of enacted and anticipated stigma of those living with HIV and have since adapted the concept to people who use drugs (Earnshaw et al., 2013). The authors define enacted stigma as "experiences of prejudice, stereotypes, and discrimination from others in the past" and anticipated stigma as "expectations of prejudice, stereotypes, and discrimination from others in the future" (Earnshaw et al., 2013, page 3). The enacted stigma that people who use drugs face from society, as well as the associated adverse effects on risk behavior and health outcomes, is well-documented. For example, research by Friedman et al. (2017) showed that after people who inject drugs experienced interpersonal attacks on their dignity, they partook in riskier health behaviors, such as needle sharing. Similarly, an Australian study found that among people who inject drugs, those who reported discrimination in the past 12 months had elevated rates of overdose, diminished physical functioning, and mental illness (Couto e Cruz et al., 2018). The primary sources of discrimination reported by participants in this study included pharmacies, doctors, and hospitals. This correlates with findings that medical providers may harbor negative attitudes toward people who use drugs and often lack sufficient training or knowledge to address their medical concerns (Merrill et al., 2002; Brener et al., 2010; van Boekel et al., 2013; Pullen and Oser, 2014; Chiarello, 2016).

Rural communities are disproportionately burdened by opioid and methamphetamine use in the United States (Ellis et al., 2018; Palombi et al., 2018; Baker et al., 2020). Stigma and other barriers to accessing medical care can be magnified in rural settings where there are fewer options for healthcare services and perhaps less anonymity in medical interactions (Jones et al., 2009; Pullen and Oser, 2014; Buer, 2020). This problem is compounded by a fear of legal consequences that can follow the identification of illicit drug use by a patient, such as incarceration or losing custody of their children (Koester et al., 2017; Latimore and Bergstein, 2017). Such legal consequences and vulnerability to discrimination and stigmatization may be exacerbated by recent changes to rules governing confidentiality of patient records in substance use disorder treatment (Knopf, 2020). Despite the profound impact that such barriers have on health outcomes, few studies have elicited the experiences and perceptions of people who use drugs regarding healthcare interactions, particularly in rural settings. Understanding the healthcare experiences of people who use drugs in rural communities can help inform interventions that improve access to, and quality of, healthcare for this vulnerable population.

Through qualitative interviews in rural southern Illinois, we explored people who use drugs' experiences with healthcare systems, particularly Emergency Departments (ED) and EMS. In this paper, we describe the barriers they faced when seeking medical care and their responses to those barriers. We also explore the role law enforcement played in their medical decisions and experiences.

MATERIALS AND METHODS

This study reports findings from qualitative data of the Delta Rural Health Study, a member of the multisite Rural Opioid Initiative (ROI) cooperative agreement (see Funding). The ROI focuses on understanding rural opioid use and the potential for HIV, HCV, and other sexually transmitted infections in nine rural regions of the United States.

Study Setting

The study was performed in the Illinois counties of the Delta Regional Authority, an understudied area with high rates of HCV infection and drug overdose (Illinois Department of Public Health, 2017). This region consists of the 16 southernmost counties of Illinois: Randolph, Perry, Franklin, Hamilton, White, Jackson, Williamson, Saline, Gallatin, Union, Johnson, Pope, Hardin, Alexander, Pulaski, and Massac. According to the 2018 American Community Survey, these counties are predominantly rural, with an average population of 20,623 and the region has substantially lower median household incomes than Illinois as a whole (United States Census Bureau, 2019).

Participant Eligibility and Recruitment

Participants had to be at least 15 years old, report injecting any non-prescribed drug or using non-prescribed opioids by any route in the past 30 days, reside in one of the aforementioned counties, speak English, and provide informed consent. Participants were recruited from three sources: (a) an indigenous local harm reduction organization (HRO) that provided mobile syringe services, naloxone and HIV/HCV/STI testing, (b) persons who completed the study's survey component and referred additional participants as part of an incentivized respondent-driven sampling approach (Heckathorn, 2011), and (c) a community-based drop-in center that primarily served people experiencing housing instability. As interview recruitment progressed, participants were purposively selected to provide variation in demographics, drug of choice, and county of residence, as well as variations in experiences with medical care among persons who knew themselves to be HCV-positive.

Data Collection

All participants completed the informed consent process. Persons incapable of informed consent due to drug withdrawal or intoxication were rescheduled. Three members of the research team conducted semi-structured, audio-recorded narrative interviews with participants using an interview guide described below. Interviewers had no affiliation with healthcare providers used by people who use drugs in the study area. Interviews took ∼45–90 min and were audio-recorded. A unique ID and pseudonym were created for each participant, and interview transcripts were de-identified. Participants were paid $40 cash for their contribution. The study protocol was reviewed and approved by the institutional review board at the University of Chicago and participant involvement was covered by a Federal Certificate of Confidentiality.

Interview Guide

The interview guide was collaboratively developed by researchers from all sites participating in the Rural Opioid Initiative and aimed to investigate sociocultural factors associated with illicit opioid or other drug use, high-risk drug and sex behaviors, harm reduction, and social network characteristics. It also explored factors impacting healthcare and social service utilization, treatment for substance use, experiences with law enforcement, and knowledge of laws regarding drug paraphernalia, naloxone (an opioid reversal agent), and overdose reporting. Specific questions regarding healthcare experiences included "Have you ever decided that you needed care, but didn't go?" and "Tell me about your most recent interaction with any doctor or other health care provider." Demographic data were collected with each interview.

Data Analysis

Recorded interviews were professionally transcribed and then reviewed by interviewers to correct transcription errors and omissions. After finishing an interview, interviewers made notes regarding the interview, including identifying potential themes. Data analysis combined structural coding (Guest et al., 2012) reflecting specific topics of interest at the study's inception and a modified grounded theory approach where themes are coded and organized as they emerge from the data (Charmaz, 2006). A primary coder developed a code book of mostly *a priori* codes based on the interview guide and then coded one transcript, refining the code book throughout the process. A second coder coded the same transcript to check for fidelity and overall consistency in the application of codes. Once these codes were agreed upon, iterative coding was conducted by the primary coder for the remaining 19 transcripts. For this study, further thematic analysis was conducted regarding participants' experiences with medical care providers, with a focus on barriers to seeking or accessing medical care and participants' responses to these barriers. Transcript coding and analysis was done in NVivo 12®.

RESULTS

Twenty participants were interviewed, their mean age was 36.6 years and the majority were white (90%), which aligns with census data for this area, and male (65%). In the 30 days before their interview, the average number of drugs used was 4.6 and over half (17) of participants had used methamphetamine. Other commonly used drugs were prescription anxiety drugs (12 participants), heroin (10 participants) opioid painkillers (10 participants) and cocaine or crack (10 participants). There are no definitive descriptions of drug use prevalence in the area studied, but our sample appears to reasonably align with substance use patterns suggested by local harm reduction providers, drug treatment programs, police drug seizures, and newspaper reports.

The primary finding is that participants reported multiple, interrelated barriers to seeking medical care. Structural, financial, and interpersonal issues often led participants not to seek care or created barriers when they sought care. Structural and financial barriers included limited nearby services, lack of transportation, and inability to pay for care. However, interpersonal factors, many of which were linked to participants' prior experiences with medical services, were described by participants as the most formidable barriers to care.

We divided interpersonal factors into three broad themes: (1) stigma, (2) inappropriate treatment, and (3) fear of negative consequences. Participants' responses to these barriers were included within each theme. We found that most of the medical services discussed were provided by EMS or EDs and their associated providers and that law enforcement interactions played an important role in participants' healthcare experiences and decisions. We use pseudonyms throughout the paper when quoting participants.

(1) Stigma

Descriptions of stigma and discrimination were pervasive throughout participants' narratives. Enacted, or past experiences of stigma, led to expectations of future stigma, which affected participants' healthcare seeking decisions.

(a) Enacted Stigma:

Participants reported being treated poorly or differently by medical providers as a result of their drug use or providers' assumptions about their drug use. Participants recalled being identified as a person who used drugs by drug testing, track marks on their arms, or the inability of staff to access veins for blood draws. After being identified as a person that used drugs, participants felt immediately stigmatized and mistreated. Sam, a 40-year-old man, described a medical interaction as "[…] horrible, horrible. They treated me like shit because they knew I was a drug user." He went on to describe what he experienced as a forced catherization.

> It was a local hospital up here in [Town A]. They treated me like shit. They obviously knew that... I had scarred veins and stuff like that… They needed me to pee for urinalysis just to see what was in my system and they said that if I couldn't... I told them I didn't have to pee but if they brought me some water that I'd be able to drink the water and give me about 15 minutes and I'd be able to pee. They brought in the water cup and they let me take one sip of it and then they asked me to pee. I told them I couldn't and they catheterized me… They held me down and cathed me, yeah… It wasn't the best experience.

Maya, a 60-year-old woman, Walter, a 33-year-old man and Sarah, a 38-year-old woman, respectively, described being treated like a "second class citizen," "piece of crap," and "drug addict" in medical settings. Maya explicitly stated "I don't like going to the ER because you're treated like a junkie." Emily, a 27-year-old woman, described an initial evaluation that she felt led to stigmatizing treatment.

> When I have had to go to the ER for anything, the first thing they do is drug test. Like if you go in for a legit reason, like something's really wrong, and the first thing they do is drug testing, like, "Well, you're not going to treat somebody that's on drugs?" They make it a point to have you drug tested and then they want to... You get treated different if you do fail your drug test in there.

These examples show how participants felt stigmatized, dehumanized, and mistreated by medical providers based on their identification as people who use drugs when they accessed care. The next section explores how past experiences of discrimination affected decisions about future utilization of healthcare.

(b) Anticipated Stigma:

Participants often described situations in which anticipated stigma, in the form of judgment or discrimination, discouraged them from accessing medical care or disclosing their drug use to providers. Rob, a 42-year-old man, described being "too embarrassed" to seek care for an injection-related abscess. Similarly, Jack, a 43-year-old man, expressed a concern about facing stigma due to a medical diagnosis when asked if anything kept him from seeking care.

> Yeah. Yeah. Because pretty much if you got hep C nowadays, it's because you were an addict. That's usually pretty much the only way nowadays that people have it. They're going to know you're an addict…I don't want to be judged.

Due to anticipation of stigma or mistreatment, participants often reported avoiding medical care. Alex, a 40-year-old man, said he would not seek care unless he was "in extreme pain," and Emily explained "I don't ever see any doctors or I try to avoid the ER at all possible costs." When asked about one healthcare setting, Walter recalled being "treated fine there, so long as it's not for drugs" but when pressed further about his experiences he responded "I try not to get sick much."

Some participants sought care but described strategically withholding disclosure of their drug use to providers to avoid judgement. As Kelly, a 30-year-old woman, responded when asked if she discloses her drug use: "No, I don't. Not until it comes down to it. Especially if... Because I don't want everybody that comes across my paperwork to read it." A few reported that they generally were upfront about using drugs. For example, Anthony, a 25-year-old white man, initially told us that he was "totally comfortable" making this disclosure, although he described providers' reactions as "disbelief" due to his "clean-cut" appearance. This description suggests that white race and a middle-class appearance can be deployed to offset at least some of the stigmatization that a person using drugs is likely to encounter when seeking medical services. However, in section 2, below, Anthony also described using a calculus to decide when to disclose.

Jack described the relationship between needing pain medication for an injury, but also wanting it for his "addictive mentality" and struggling with how much to tell his providers in order to be treated like a patient and not an addict.

> So, I need to go get stitches. Me not wanting to look like an addict, but at the same time I knew I was in pain then and I knew I'd be in pain after they'd put the stitches in, so I wanted pain pills, and my addictive mentality wanted the pills too. Over the years, I have been looked at, looked down on because I was an addict and treated different in a hospital. I don't think that's right. Your job is there to treat the problem but you had so many addicts going in there and trying to work the system to get free pain pills… That makes it look bad for the people that actually kind of need them… Myself included, I've done it myself. Went and said I had a backache or a toothache and nothing was on me just so I can get pain pills… But then when you need them, you don't want to ask because then if you already know what you're talking about and what you're asking for, they'd pretty much know you're an addict, that's some con… They do treat you different.

Overall, between enacted stigmatizing behaviors by medical providers, and the anticipated stigma that participants felt they would face in medical settings, stigma played a key role in participants' medical decisions and acted as a barrier to seeking care and disclosing important health information.

(2) Inappropriate Treatment

Participants described experiences in which they felt their medical issues were undertreated or inappropriately treated because of their drug use, particularly regarding pain management.

Participants described not receiving the medical attention they needed and providers not taking their pain or medical concerns seriously. Sometimes participants felt they were undertreated because providers assumed that they were seeking drugs. In response, Anthony said that the decision to disclose his drug use depended on the reason he was seeking medical care: "Yeah, so I don't know, it just depends on what the reason that I'm going. If I'm going because I have respiratory issues going on, I'm going to tell them the truth. If I go there because I broke a rib, I'm going to lie."

Other participants attributed their poor care and follow up to providers' perceptions of them as drug users and their past experiences of stigmatization in medical settings. For example, Matthew, a 27-year–old man, described long wait times and frustrating results from his local emergency department.

> Like I said, you don't get, you can't go in off the street and get real care there… You can't, it's very, very hard to go to that ER without being there for two or three hours and walking out with nothing other than more resentment, more frustration and pain and anxiety and feeling more wronged and more dehumanized and less trust and faith in your own nation. Honestly, every day of my life, I'd give anything just to have real healthcare and real support health wise.

Kelly described experiences of visiting multiple hospitals in unsuccessful attempts to receive adequate care.

> Oh, I mean just in general. We call [facility A] the band aid hospital. Sometimes they give us our kind of band aid and push them on their way. Other hospitals give our… We end up leaving that hospital and go straight to another one because they're still bleeding, and they give them a suture or two, or something like that.

While some participants described having sought pain medication from EDs or other providers when they were not in need of medical treatment, they also described situations in which they were in considerable pain from legitimate medical conditions but felt they were not treated appropriately because of their drug use history. For example, Maya explained, "you go to the hospital and they won't so much as give you a pain shot because they see track marks and they think you're fishing for pain medicine, when you're in legitimate pain."

Other participants described specific situations in which they believed their medical issues had been undertreated. Trevor, a 38-year-old man, described being left "on the back burner" at an ED when he tried to receive care for a neck abscess. He also stated that ED staff were "profiling" to determine who to give pain medication to: "If you're older and you look straighter, if you look fine, good cleaned up and look fine, they'll give you [pain medication]." In another example involving mental health, Allison, a 38-year-old woman, described self-medicating in response to the long wait times to see a psychiatrist: "Here, you can't get into one for months at a time and people have got to get rid of that, that whatever, anger, hurt, and dulling it is the easiest way to do it. It's easy to do with drugs." David, a 39-year-old man, spoke of the risk of being denied medical care all together because of drug use: "they might not treat you after they find out you're on drugs." Overall, as Evan, a 57-year-old man explained about his local hospital, a general sentiment was that hospitals "ain't doing shit" for the medical concerns of people who use drugs.

There were a few examples in which participants perceived they had been inappropriately treated with psychoactive substances by medical providers. Megan, a 38-year-old woman, expressed that she felt a provider had overprescribed her anti-anxiety medication that she did not need at the time. Kelly noted cutting the dosage of her opioid prescriptions in half because her providers gave her dosages that were too high. She went on to describe medical providers as "Pez dispensers." In another example, David, who primarily injected methamphetamine, described convincing a nurse to inject him with his prescribed pain medication in a rehabilitation facility because it did not work fast enough when he took it orally.

> And so they started with the therapy really intense, and it hurt. It hurt so bad, and just taking the pills just wasn't fast enough...I talked one of the nurses into breaking one down for me. And she injected it for me for the first time. And it worked. So she started breaking them down for me, and I started injecting myself. After 6 weeks of doing this, they released me from the hospital, and they put me through pain therapy, and they took me off of it, and it was hell. Started looking for them on the street.

A common result of these negative experiences as expressed by participants was to lose faith and trust in their medical system. As Anthony described about providers, "They cover each other's asses. I don't like it. They're not… I just don't trust them, and for good reason." Matthew described his feelings that medical providers are more worried about their livelihoods than their patients and that medical institutions' financial concerns are more important to them than patient care.

> They don't care about people at all. They care about the student loans they had to take out to go to school to work at that hospital taking care of other people. I see it every day and it just breaks my heart.

When participants felt their medical concerns were ignored or they were inappropriately treated, they chose to hide their drug use from providers, treat themselves, or give up on the system and avoid accessing care all together.

(3) Fear of Negative Consequences

Another barrier to accessing medical care was a fear of negative legal and social consequences. These consequences came in two general forms, the most common was a fear of law enforcement involvement due to participants' drug use. This fear was often cited when EMS responded to an overdose. The other form was a fear of breaches in participants' confidentiality, which could harm their reputation in their communities. We found that these fears were often rooted in both past personal experiences and the experiences of others known to participants.

(a) Fear of law enforcement involvement in medical interactions:

Participants described fears of encountering law enforcement and possible arrest when seeking medical care while they had drugs in their system or were carrying drugs. Ryan, a 35-year-old man, explained that he never goes to the doctor when he has drugs in his system because "(I) don't want to be investigated." Trevor described overdosing and begging not to be taken to the hospital because "I had meth on me." When asked about how she decides when to access care and how she is treated in local ERs, Emily stated she avoids the ER "at all possible costs" and reported a time that her brother sought medical attention and was arrested for drug possession in the ED.

> My brother actually went to the ER. I don't even remember what he went for. And they drug tested him and they called the cops on him. And they're not even supposed to do that. And he ended up going to jail because they called the cops because he failed his drug test and they didn't like him anyways… But, they called the cops on him and then the cops come up there and searched him at the hospital. And he had drugs on him, so he went to jail.

Heather, a 31-year-old woman, was convinced that if she sought medical care with drugs in her system, her medical test results would be shared with law enforcement

> I haven't been to the doctor in a long time. When I'm on meth, I don't go to the doctor. You go... if you go to the doctor on meth, and they drug test you, then they fucking file a report with the police, like every fucking time.

Sarah reported not wanting to be treated by a specific ED provider who had previously let police officers into the area where she was being treated because the provider believed she was lying about the causes of her injuries.

In another form of medical service and law enforcement interaction, Maya and Kelly described experiences in which police officers took their legal medications or legal prescription slips from their homes or cars during searches. In both cases, the participants' access to legally prescribed medications was delayed. These actions were seen as disrespectful and dehumanizing, as they suggested that law enforcement concerns outweighed medical care.

Based on personal or second-hand experiences, participants' felt that law enforcement was frequently inappropriately included in their medical care and that accessing medical care, especially while using drugs, would lead to their arrest or investigation.

(i) Fear of calling EMS for an overdose:

Most fears of law enforcement involvement in medical interactions regarded accessing EMS in response to an overdose. While many participants described themselves as willing to call 911 despite experiences or fear of arrest, they recounted others' unwillingness for the same reasons due to, as Anthony put it, a "culture of fear." Multiple participants recalled situations in which EMS was not called when a person was overdosing. The decision to avoid calling 911 was almost always attributed to fear of legal repercussions. Kelly describes one of these instances:

> His whole body was swelling up, his feet, his arms, everything. I told everybody 'I think he's overdosing.' But nobody had a car to take him to 911. The other people I was with didn't want 911 called because they were at a house that had a bunch of drugs at it.

When EMS was called for an overdose or any other reason, police officers were said to be the first to respond. Participants felt that in these situations law enforcement was often more concerned with arresting people or finding evidence for arrests than with addressing the emergency that prompted the call. For example, Emily described being arrested due to an outstanding warrant for a missed court appearance when she called 911 for a friend who had overdosed. Maya described a situation in which police officers first searched her house instead of administering CPR or naloxone while she was overdosing.

> They've been called here numerous times that I've overdosed. Cops have to show up before the ambulance. One time, I was sitting in that chair and I was turning bluer and bluer and [husband] called 911. They came in and they said, 'Well you're going down for homicide,' to [husband]. He says, 'I don't care what the fuck you arrest me for. Get her to a hospital. She's turning bluer.'…They sat there and they started searching through the house, dumping out the garbage can in the bathroom and he said, 'Hey, I didn't give you permission to go through my house. I called 911 to take my wife to the hospital.' …But I sat there for 20 minutes while they argued with [husband], turning bluer and bluer.

Some participants expressed negative attitudes toward EMS, either because they associated them with law enforcement, or felt they behaved as law enforcement rather than medical providers. Sam described not calling EMS when a friend was overdosing because "I just don't like law enforcement at all." Matthew explained, "EMTs, people who drive and operate ambulances and go to the scenes of crashes and crimes, they need better bedside manner. Every day people are suicidal and having panic attacks and anxiety attacks. When the ER shows up and they act like fucking cops. The cops in this town have more of a bedside manner than the ambulance people."

Despite these negative experiences, Anthony believed the police had been treating people better since they had been trained to deliver naloxone to those overdosing: "They're trained more to worry about saving this person's life instead of worrying about what fucking…Ted or Alan's got in his fucking cabinets." However, Anthony also believed a police officer administered CPR improperly to an overdose victim because "you don't want to get a little fucking junkie fucking saliva on your mouth?" Another participant, Walter, described waking up from an overdose in jail, rather than in a hospital: "they had to hit me like six times with [naloxone] and found out I had a warrant so (I) came to in jail."

Overall, fear of law enforcement involvement, leading to investigation or arrest, was a factor in many of participants' decisions around medical care, and often acted a direct barrier to accessing care, particularly when calling EMS for an overdose.

(b) Fear of breaches in confidentiality:

Another feared consequence that served as a barrier to accessing medical care was that private medical information would be inappropriately shared by medical providers. This was especially relevant given the rurality of the area and the small-town nature of the communities described throughout participants' narratives. For example, when asked if he is worried about a local provider performing his STI testing, Evan expressed concern that his test results may be shared by the local health department. His response suggested that he is skeptical about the confidentiality of his test results when local health departments communicate with each other about disease outbreaks.

> Yeah, they rap a lot. It's like, let's say, [Town C], [County A] get a big case of AIDS, like how they know that? A person that may have it they don't go advertising it. So that's some people talking. So, you be skeptical about going to these places around here.

Two participants, Rob and Emily, described experiences in which their confidentiality was breached by medical providers. The first involved a receptionist who Rob believed disclosed his HIV status to the entire medical staff "so when I walked out they all turned around, looked…" This experience caused Rob to feel "very hesitant of who I share my status with when it comes to medical offices because of that situation." The other breach came in the form of a provider disclosing the content of Emily's counseling sessions to community members.

> I try to avoid conversation like that, because I was seeing a counselor in [clinic name] a couple of years ago, and was talking to them about everything going on in my head and the pills… and all that stuff was supposed to be confidential, and she actually told... she said something about it to numerous people. People were coming to me saying, "Is this your counselor at [clinic name]?" I was like, "Yeah." And they said, "Well, she's telling people everything you say in there." And she even went to my mom with it too. She told my mom certain things… Yeah. So I tried... that's something that I really try to avoid talking to people about. That's really the last thing I need to get out. And I think that that's why I've not really went to rehab or tried to go to rehab to get help.

Emily explained that she chooses not to disclose her drug use now to providers because of that experience. These two experiences describe how past negative medical experiences directly affected participants' future decisions regarding seeking care and disclosing important health information to providers.

DISCUSSION

Trust in a provider is vital to the health and well-being of the patient. Trust allows for a shared decision-making process regarding medical care, which has been shown to improve health outcomes (Peek et al., 2016). In our analysis, we found that participants felt that providers often breached this trust through stigmatization, mistreatment, involvement of law enforcement, and violations of confidentiality. We also found that the blurred relationship between the criminal justice and healthcare systems in these communities fostered mistrust in the intentions of medical service providers and created, as one participant described a "culture of fear" that affected participants' healthcare decisions. Our participants made it clear that these breaches in trust discouraged them from accessing medical care and, when they did access care, from disclosing their drug use, associated risk behaviors, and even previous medical diagnoses to medical providers.

Our study adds to the limited body of research that qualitatively explores the experiences of people who use drugs with healthcare services. Previous works have studied different healthcare service types, generally have not interviewed people who actively use drugs or were conducted in large urban centers (Earnshaw et al., 2013; McKnight et al., 2017; Paquette et al., 2018; Biancarelli et al., 2019). Our study contributes to the literature by investigating the experiences of people who actively use drugs when navigating multiple rural healthcare settings including EDs and EMS, but also with mental health, infectious disease and primary care providers.

Although many of our findings reinforce the current literature on the stigma people who use drugs experience in healthcare settings, we also found concerning new themes that warrant further investigation. Our study reinforces previous work that shows people who use drugs are fearful of utilizing EMS for an overdose due to the possibility of arrest (Koester et al., 2017; Latimore and Bergstein, 2017). This finding is important as many of our participants' healthcare interactions began with a call to EMS, to which law enforcement was often the first responder. Wagner et al. (2019) similarly found that people in urban areas who use drugs equated a 911 call for a medical reason to calling the police. Our study found that this sentiment may be exacerbated in rural settings where our participants were often well-known to a small police force and, not uncommonly, had ties to some officers through shared school histories, neighborhoods or family relations.

Our study also shows how this fear extends to EDs and other healthcare settings, with greater consequent negative impact on healthcare decision making than previously reported. This fear is likely to be intensified by recent regulatory changes to the way patients' substance use disorder treatment information is stored and shared (Knopf, 2020). These new rules allow opioid treatment programs to input patient information into Prescription Drug Monitoring Programs (PDMPs), which law enforcement has the potential to search, as well as expand the circumstances under which patient information may be shared with law enforcement. The concern is that these new rules will discourage patients from seeking opioid use treatment in order to avoid persecution and discrimination. Studies have shown that law enforcement interactions increase rather than decrease health risk behaviors such as injection initiation and syringe sharing (Melo et al., 2018; Park et al., 2019) and that law enforcement involvement in the life of a person who uses drugs is almost unavoidable in the U.S. (Winkelman et al., 2018; Green et al., 2019). Therefore, a closer look at the way these interactions occur in rural medical settings and for medical purposes is critical to ensure that the rights of people who use drugs are upheld and their health is prioritized.

Our examination of the experiences of people who use drugs in rural southern Illinois uncovered a broad array of problems, from stigmatizing attitudes, loss of privacy, and poor care to active harm at the hands of their caregivers. While all served to diminish patient trust and confidence in the healthcare system, these diverse experiences reflected a multitude of failures along the cascade of providing a therapeutic interaction for people who use drugs. We suggest several potential interventions to address this range of issues:

First, reinforcing basic principles of confidentiality in patient-provider interactions within healthcare settings, especially as they apply to law enforcement, could begin the process of rebuilding trust between people who use drugs and the healthcare system. This exercise will be difficult, as law enforcement's rights in healthcare settings are often ambiguous and vary across the country (Jacoby et al., 2018). As a result, the American College of Emergency Physicians, along with researchers, have called for clear, universal guidelines, and policies for EDs, which could be developed with the input of community members (Tahouni et al., 2015; American College of Emergency Physicians, 2017). If implemented, policies could be communicated using signage and language in clinic and hospital handouts and posters clarifying protocols regarding protected health information (PHI) and law enforcement involvement. The signage could also convey positive messaging for people who use drugs, encouraging their access of healthcar,e and use of harm reduction services and practices.

Second, trainings on common diseases and complications faced by people who use drugs and the important public health consequences of these conditions may offer healthcare providers the tools, knowledge, and motivation to focus on best-practice treatments for this population rather than react to their stigmatized behaviors and appearances. These trainings can include direct stigma training, which has been shown to reduce stigmatizing attitudes by healthcare providers in the care of people living with HIV and may be equally efficacious in changing attitudes toward people who use drugs (Stringer et al., 2016). The use of trauma informed care (TIC) should also be incorporated into these trainings, which emphasizes understanding and responding to behavior through the lens of trauma, as well as cultural sensitivity and focusing on patients' safety and control in their medical interactions (Bassuk et al., 2017). TIC has been recommended in the treatment of all marginalized communities, and would be especially important in people with substance use disorders who have been shown to experience high rates of trauma (Konkolÿ Thege et al., 2017).

Third, the development of referral systems, especially out of EDs, to link people who use drugs to drug treatment and harm reduction services is another important step. Referrals that enable same day intake and treatment initiation, i.e. warm-hand-offs, are especially likely to improve patient follow-up and outcomes (D'Onofrio et al., 2015, 2018; Ahmed et al., 2019; Kelly et al., 2020). Recent work has also found success in incorporating telehealth and text messaging into referral systems to help with patient follow up, which may be especially useful in rural settings (Kmiec and Suffoletto, 2019; Wootton et al., 2019). Such approaches could be a major step in fostering therapeutic alliances between providers and people who use drugs. Lastly, an important step is expanding harm reduction services for persons not ready or able to enter drug treatment, especially syringe exchange programs, which have been associated with less stigmatizing care and reductions in infectious disease rates (Bluthenthal et al., 2000; Huo and Ouellet, 2007; Walters et al., 2017). Giving providers the resources to properly address the medical concerns of people who use drugs could facilitate more positive, open, and productive relationships with these patients.

In regard to the criminal justice system, many interventions are being developed across the country that, if implemented in these communities, may help improve trust in law enforcement among people who use drugs. One potential strategy used in Massachusetts includes post-overdose outreach by police officers and firefighters who helped connect persons who overdosed to care and support (Koh et al., 2018). The Law Enforcement Assisted Diversion (LEAD) and Angel programs, which have already been adopted by 20 sites and 28 states, respectively, are proven to reduce drug arrest charges in participating departments (Koh et al., 2018). These are two of many ways systems in rural communities can change to prioritize health over arrest for people who use drugs and, in turn, improve community health. However, the particular nature of these interactions in rural areas must be considered when adopting any new policy or process. Other research suggests, and our findings confirm, that people who use drugs may be unwilling to call 911 in the first place, especially if they know and have had negative interactions with local officers. Interventions in rural communities may benefit, therefore, from developing a separate contact protocol for any diversion or referral programs, rather than initiating the process through a 911 call or visit to police department, like some current models. Alternatively, a 911 call for an overdose could initiate both a police response and an advocate response, in which trusted harm reduction personnel are simultaneously called to the scene and can facilitate communication and diversion. Finally, an option may be to limit the scope of police when responding to drug overdose calls, prohibiting them from searching for drugs and narrowing the conditions for which people could be arrested at the scene, such as violent felonies. Ultimately, with or without the adoption of diversion programs, our data makes it clear that the current EMS protocols for drug overdoses are contributing to more morbidity and mortality in this population by instilling fear and distrust in the system, and need to be improved.

In terms of the larger structural and environmental forces that may impact the high utilization of emergency services in this population, respondents did report barriers to accessing general medical care including lack of transportation, long wait times to see providers, and the cost of care. Infrastructural and workforce challenges, particularly in rural areas, have been well-documented in prior work, and can be addressed through expanding and diversifying delivery care models such as community health workers, pharmacy-based care, and telehealth, as well as optimizing existing provider capacity through peer network supports such as the Extension for Community Healthcare Outcomes (ECHO) program and hub-and-spoke programs for medication for opioid disorder (MOUD) treatment expansion (Komaromy et al., 2016, 2018; Speyer et al., 2018; du Toit et al., 2019; Rawson et al., 2019; Darfler et al., 2020).

Our study has several limitations. Given the lack of racial diversity of our participants and the limited geographic area, these findings may not be transferable to all people who use drugs in this or other rural regions. As the perspectives of people who use drugs are understudied in regard to healthcare services, we believe a small number of in-depth, qualitative interviews were warranted to explore basic themes and guide future research. Notably, we do not explore the perspectives of medical providers in this study, which may limit our interpretations and suggestions for interventions. Many of participants' experiences with inappropriate treatment and some of their interactions with law enforcement may have had legitimate medical or legal standing. However, regardless of the clinical or legal reasoning, these interactions left participants feeling dehumanized and fearful and affected their future medical decisions.

CONCLUSION

Drug overdoses, mental health concerns, and skin and soft tissue infections are some of the common conditions that bring people who use drugs into healthcare settings. These medical complications are often stigmatized as being self-inflicted due to their connection to illicit drug use, yet they provide an important opportunity for intervention, referral, and to establish care that can benefit the individual, their families and the communities in which they reside. Breaches of trust threaten those opportunities, which could lead to more serious health consequences including disease outbreaks and deaths. People who use and inject drugs face daily obstacles and discrimination in many facets of their lives. Rather than acting as a reprieve from stigmatizing interactions, healthcare systems often reinforce them. Our study illuminates the perspectives and experiences of people who use drugs when they engage medical services. Further research is recommended to inform interventions with the potential to improve clinical services and overall health outcomes for people who use drugs.

DATA AVAILABILITY STATEMENT

The datasets presented in this article are not readily available because analytical requests for the data must be submitted to the University of Washington Rural Opioid Initiative Data Coordinating Center. Requests to access the datasets should be directed to Mai Tuyet Pho, mpho@bsd.uchicago.edu.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by University of Chicago Biological Sciences Division Institutional Review Board. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

KE, SW, MP, LO, JE, and SF contributed to the conception and design of the study. KE and LO conducted the study interviews. KE and MP coded the study interviews. JE collected the study data and performed the demographic analysis. KR contributed to data analysis and preparation of the manuscript. KE wrote the first draft of the manuscript. All authors contributed to manuscript revision and read and approved the submitted version.

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"I'm Going to Stop Myself Before Someone Stops Me": Complicating Narratives of Volitional Substance Use Treatment

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Background: Often people assume that entry into drug treatment is a voluntary action for persons who use drugs (PWUD). This narrative informs the organizational and regulatory structure of most treatment programs and consequently affects patients' ability to exert agency over their own treatment. Yet, this view ignores the complex interplay between individual and structural factors in peoples' decision-making processes, particularly among people who use drugs who are stigmatized and criminalized. Treatment programs that assume voluntary entry may lack appropriate services for the populations of treatment seekers that they serve.

Methods: This paper uses semi-structured interviews with 42 participants in Opioid Substitution Treatment (OST) (including patients, clinic doctors and staff, and advocates) informed by one of the author's own lived experience in OST, to examine patients' treatment decisions, and in particular, if and how, the structural context of drugs' illegality/criminalization affected their willingness to pursue treatment. A Critical Discourse Analysis was used to identify key themes.

Results: Interview data demonstrates that most people who use drugs enter treatment under constrained conditions related to drugs' illegality. Themes that emerged included: 1. A feeling of limited choices due to drugs' illegality; 2. Peer and family pressure; 3. Fear of losing children; and 4. Internalized stigma (i.e. feeling they are dirty or bad for using).

Conclusion: Narratives that frame PWUD's treatment decisions as volitional provide political cover to policies that criminalize PWUD by obscuring their effect on PWUD's treatment decisions. Treatment models, particularly those that serve highly criminalized populations, should be re-conceptualized outside of normative narratives of individual choice, and be broadened to understand how larger structures constrain choices. By looking at macro-level factors, including the interplay of criminalization and drug treatment, programs can begin to understand the complexity of PWUD motivations to enter drug treatment. Recognizing the role of the War on Drugs as a force of oppression for people who use drugs, and that their treatment decisions are made within that setting, may enable people in treatment, and providers, to develop more productive ways of interacting with one another. Additionally, this may lead to better retention in treatment programs.

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INTRODUCTION

Entry into drug treatment is usually conceptualized as a voluntary, unconstrained action taken by people who use drugs (PWUD) and intended to rectify (i.e., treat) the problem of "addiction." This is evident not only through clinic descriptions that specifically state that their services are voluntary (University Hospitals, 2020), but also through the Substance Abuse and Mental Health Services (SAMHSA)'s Federal Guidelines for Opioid Treatment Programs which states that clinic physicians must receive "voluntary, written, program-specific informed consent to treatment" before patients can be medicated (SAMHSA, 2015: 24). The Recovery Oriented Systems of Care model adopted by SAMHSA in particular relies on presenting MMT as a "voluntary, self-directed, ongoing process" (2015: 39). Yet, this view may ignore the role of larger structural forces such as criminalization and the War on Drugs, in the lives, and treatment decisions, of PWUD.

Although research demonstrates that many people become involved with methadone maintenance treatment (MMT) as a way of avoiding harm associated with illegal substance use, rather than substance use itself, this view is rarely part of how treatment is institutionally conceptualized or organized (Frank 2018; Frank, 2020). Similarly, stigma–both from family, friends, and co-workers, as well as internalized stigma by patients themselves, also play a prominent, and potentially coercive, role in peoples' decision to enter MMT (Woo et al., 2017; Paquette et al., 2018).

Since most treatment providers conceptualize patients' decisions to enter treatment strictly through individually focused models, they may lack an appropriate understanding of their patients' needs, and thus be less equipped to serve them. For example, since most clinics see their patients strictly as "addicts" with a medical/moral problem in need of fixing, they often employ a top-down, and often punitive approach aimed at changing patient behaviors and beliefs rather than providing services designed to reduce harm in their lives (Frank, 2020).

In response, this article uses qualitative data to examine if, and how, OST patients' descriptions of treatment uptake evince constraint in their decisions. We focus in particular on how the following themes: 1. A feeling of limited choices due to drugs' illegality; 2. Peer and family pressure; 3. Fear of losing children; 4. Internalized stigma (i.e. feeling they are dirty or bad for using) complicate notions of patient agency and volition in their treatment decisions. Lastly, we argue that by acknowledging such macro-level factors and how they interact with treatment decisions, programs can better organize their services to meet the complex set of issues their patients are facing.

BACKGROUND

MMT has been extensively studied for more than 50 years and is considered to be the "gold standard" for reducing substance use as well as many of the harms associated with illegal substance use (Fareed et al, 2009; Schilling et al., 2016; Joseph et al., 2000). Studies have demonstrated its association with reduced rates of crime; overdose, arrest, and transmission of disease (Bell and Zador, 2000; Shi et al., 2007), as well as enabling individuals to live more stable and less risk-involved lifestyles (Joseph et al., 2000; Ball and Ross, 2012). The number of people on MMT has increased from approximately 227,000 in 2003 to over 350,000 in 2015 (Alderks, 2017).

Despite its many benefits, MMT is generally unpopular with PWUD as demonstrated by its consistently low rates of retention (SAMHSA, 2017). According to the United States treatment Episode Data Set, the median length of stay in Medication Assisted Opioid Therapy, generally considered to be a maintenance-model to be used indefinitely, is only 100 days (SAMHSA, 2017). Many have argued that this is partly because MMT, in the United States, is over-regulated, punitive, and organized according an abstinence-only philosophy which is at odds with the needs of many of those using it (Joseph et al., 2000; Harris and McElrath, 2012; Strike et al., 2013). For example, scholars have suggested that a large portion of the patient population are using the treatment, at least in part, as way of reducing the harms of active substance use, caused mainly from the illegality of drug use, rather than as a means to become abstinent (Koester et al., 1999; Harris and Rhodes, 2013; Frank 2018; Frank, 2020). Conceptualizing problematic substance use through the lens of "addiction" has also been criticized by many scholars (Hart, 2017; Fraser et al, 2014; Keane, 2002; Reinarman, 2005), however this narrative is not only dominant culturally, but also informs the organizational and regulatory structure of most treatment programs in the United States (SAMHSA, 2016; White and Mojer-Torres, 2010).

Thus, there is substantial evidence to complicate overly simplified notions of patient volition in regard to substance use treatment and to justify further investigation into this important aspect of treatment. Gaining a better understanding about patients' motives and experiences with MMT is essential to maximize the benefits of MMT and reach larger numbers of PWUD.

METHODS

This article is based on two years of qualitative research originally conducted by Frank and including both semi-structured interviews and 2 years of ethnographic observations (Reeves et al., 2008). All data has been anonymized and participants are referred to by pseudonyms. All participants provided informed consent and the study was approved by the City University of New York, The Graduate Center Institutional Review Board.

Recruitment

Frank recruited participants using a combination of purposive and snowball sampling based initially on contacts maintained through his previous experience as a PWUD and as someone on MMT (Panacek and Thompson, 2007). He had used illegal opioids regularly from approximately 1994–2005 in multiple cities including Chicago, IL, New York, NY, Sheffield, United Kingdom, and Portland, OR, and has been in MMT since then at two separate clinics: one in Chicago, IL and one in The Bronx, NY. In some cases, participants were sought out specifically for their unique perspective on the study's themes, for example, individuals with expertize on the harm reduction resources in New York City. In other cases, participants were recruited in the process of ethnographic observations or through social networks at harm reduction locations. These participants often recommended friends and/or acquaintances to participate. Attempts were also made to recruit participants from a variety of racial, ethnic, and gender groups, however, because of the often-spontaneous nature of the interviews we were not able to collect accurate demographic information for all of the participants. In some cases, participants were already friends and acquaintances who Frank remained in touch with following the study. This is also how he became aware of the more recent circumstances in the participant, Jenny's, life. Participant recruitment was stopped at 42 because saturation was reached at that point.

Data Collection

Data was collected in New York City from 2014 through 2016. Frank conducted semi-structured interviews with 42 stakeholders including patients (individuals who had been on MMT for at least 1 year), treatment providers (including Clinic Directors, doctors, counselors), and substance use/treatment advocates (people who were involved with organizations that advocate for people on MMT such as the National Alliance for Medication Assisted Recovery or for the rights of people that use drugs such as the International Network of People that Use Drugs). Interviews lasted approximately 1 h, and were recorded and transcribed by Frank later.

Although interview questions varied by participant category, they each addressed participants' experiences with, and views of, illegal drug use and treatment. The following domains were addressed: motivations for participation in MMT (either their own motivations or their perceptions of others in the case of treatment providers); recovery (what does it mean to participants; how should it be conceptualized in MMT); clinic organization (rules and regulations; focus on abstinence versus harm reduction); substance use treatment (how well does treatment meet the needs of participants; how should it be organized). Interviews, particularly with MMT patients, tended to be highly unstructured, often taking the form of a dialogue. This was important for two related reasons. First, people on MMT are by definition a marginalized group who are used to exercising caution in regards to what types of information they disclose. For example, admitting to using illegal substances or otherwise acting in ways outside of institutionally accepted behavior can result in serious penalties including dismissal from their clinic. This meant that part of the conversations, particularly early on, involved Frank's having to gain participants' trust.

In most cases, Frank revealed his own status as a person on MMT to participants. Although he had initially planned to not reveal any personal information, it quickly became apparent that the benefits of disclosure, in terms of richness and quality of data, as well as the increased honesty and comfort of the study participants, far outweighed the benefits of not "biasing" the data. For example, participants often visibly relaxed or verbally expressed relief upon Frank's disclosure. Similarly, the familiarity with terminology, common culture, and shared experiences, also helped to position him as part of the community rather than an outsider, who are often (and with good reason) viewed with suspicion.

Secondly, because ideologies of oppression are often internalized (Gorelick, 1991; DeVault, 1996; Reinarman, 2005)—particularly in an institutional setting like MMT (Goffman, 1968; Foucault, 1972; Harris and McElrath, 2012) - it is likely that participants from this group may initially describe their experiences through the institutionally accepted narrative, regardless of how well it aligns with their experiences and/or treatment goals. The dialogue interview format helped to create an environment where participants felt more comfortable describing their experiences in ways outside of those concepts and language.

These types of methodological concerns, which necessarily address internalized power structures and the ideologies that support them, have often been discussed in Marxist and Feminist research (Powers, 2001; Bloom, 1998). For example, numerous feminist scholars, particularly those working with qualitative methods, have rejected the notion of a distanced and neutral observer, choosing a situated approach to knowledge instead (Haraway, 1988; DeVault, 1996). Situated approaches are those that acknowledge the positionality and power relationships existing between researcher, subject, and participant. They are most often used when studying groups that are structurally and/or ideologically marginalized, and generally place a greater emphasis on transparency and reflexivity than on neutrality and objectivity. Situated approaches to research are also more comfortable with the political and activist concerns of research, in that challenging power is seen as a valuable part of the process (DeVault, 1996). Addressing these tensions, feminist scholar Marjorie L. DeVault writes that situated approaches "provide the outline for a possible alternative to the distanced, distorting, and dispassionately objective procedures of much social research." (1996; p. 29).

Frank also made ethnographic observations in New York City methadone clinics and harm reduction organizations for approximately 2–4 h a week for a period of approximately 6 months. During observations, Frank engaged in discussion with various individuals and assessed the general atmosphere of each location. After each observation period, Frank made notes that were later used to develop study themes.

Data Analysis

Data was originally coded by Frank for themes using AtlasTi, a software package used for qualitative data analysis. Later on, when the two co-authors agreed to pursue this research question, data was then analyzed by both authors in an iterative process informed by previous literature as well as themes that emerged throughout the research process. Themes included: the role of a substances' legality/illegality in people that use drugs' treatment choices; the role of stigma in people that use drugs' treatment choices; and fear of disrupting family relationship in people that use drugs' treatment choices; as well as others. Authors met regularly (by phone and Zoom) to discuss the study's primary themes and focus.

In line-with Frank's situated approach to data collection, the authors utilize a Critical Discourse Analysis (CDA) approach to the analysis of the data (Fairclough and Wodak. 1997; Fairclough, 2013). CDA, an approach often used in Foucauldian-inspired work, utilizes narratives deployed by different stakeholders, as means of revealing hidden power structures, oftentimes in order to problematize dominant cultural and/or institutional theoretical models of behavior (Van Dijk, 1993; Cook, 2005). In "Discourse Analysis and the Critical Use of Foucault," Linda Graham describes Foucauldian forms of discourse analysis by their concern with understanding power, representation, and a reticence to see method as an objective means of uncovering "truth" (Graham 2005). She writes that such an analysis would focus on "constitutive and disciplinary properties of discursive practices within socio-political relations of power" as a way of illuminating "how language works not only to produce meaning but also particular kinds of objects and subjects upon whom and through which particular relations of power are realized" (Graham, 2005: 4).

In practice, this meant that both authors discussed the interview texts with an aim to uncover and describe how they fit within larger systems of power, such as drug prohibition and the War on Drugs. Since the two authors occupy different positions (gender, ethnic, personal history) in relation to the subject matter, we used this as a check against leaning too far into either of our positional biases and often discussed the data from a variety of perspectives.

RESULTS

Limited Choices due to Drugs' Illegality

The illegality of heroin (and illegally used prescription opioids) structured and affected the lives of participants and in particular, their decisions about treatment. Nearly all participants focused, to some extent, on how the illegality of heroin affected their decision to attend MMT.

In some cases, this consisted of formal pressure exerted on participants by the Criminal Justice System (CJS). For example, courts sometimes gave participants a simple choice between jail or treatment. Participants described their experiences with courts as confusing, and many were unsure exactly what they were agreeing to. They simply knew that they were avoiding incarceration. For example, Foster, a black man in his early forties, who has been on MMT twice, describes how he became involved with MMT in this way:

> "Basically, I felt that I was being chained. At the time, beginning with the courts, [they] had made me get on the program, to do their protocol . . . I had to get on it [MMT] or else go to jail . . . Between that with parole, the courts and all that, all that combined in one. So I was forced on it. So I really didn't really like it at the time, didn't understand it anyway." (Foster, 2014)

Here Foster describes a situation where he felt he had little choice, and the overarching goal was to avoid jail. He said that he was "made" and forced into treatment, connoting a lack of free will and agency. He also mentions that he did not understand what he was agreeing to, eluding to another erasure of free will. Involvement with the CJS for most participants, like Foster, was experienced as overbearing, threatening, and confusing and often gave participants the feeling of having little control over their own situations. Literature on the CJS has noted the use of such techniques as a form of social control (Clancey and Howard, 2006; Tiger, 2013).

Participants involved with the CJS also described using treatment as a strategic means of avoiding more severe forms of punishment. For example, some individuals utilized treatment as a way of demonstrating their desire to abstain from drug abuse to judges in order to avoid jail. Thus, even those who didn't describe their experience as "forced" still describe a context of constraint that significantly reduced their agency and made this kind of legal maneuvering necessary. For example, Monica, a white woman in her 30 s describes her experience like this:

> "I wasn't forced [but] I had legal issues, I was incarcerated for like 28 days and basically was put into a 28-day program since I had never done any treatment programs before . . . . . .Basically the judge, I was in jail a week, and they were like, "If we get her in a program, she can leave right now." . . ..But of course no one is in a hurry. I'm in a hurry, I'm like, "Get me in a program now!" But I can't call anybody, whatever. So anyway, I just ended up sitting there until somebody decided that they had a place for me to go. And basically, somehow I made the methadone clinic seem a little bit more than what it really was and the judge was like, "Wonderful," and he considered that outpatient, he overlooked the fact that I was taking Methadone Maintenance Therapy. I was like, "I go to groups, I see my counselor once a week." I played it up, I sold it and that was fine. Everybody was like, "How did you get methadone maintenance as an outpatient?" I'm like, It worked. So basically, I did have to do an outpatient and they dismissed the charges, everything. I had two felonies and three misdemeanors and I plead out to disorderly conduct." (Monica, 2014)

Monica's account also demonstrates how participants evinced agency in the face of constraint. She recounts skillfully convincing a judge to dismiss her charges and even reports having exaggerated the role she believed methadone would play in her life to get an outcome that she preferred. Thus, despite the many forces of constraint that she describes, for Monica, this was a form of ascertaining her agency, and a way for her to be in control of her life.

However, participants did not always become involved with treatment as a result of direct institutional pressure. Many described indirect pressure because of a constant risk from law enforcement that made holding a job, going to school, or establishing a stable life extremely difficult. Others described their reasons for pursuing treatment as being "sick of the hustle" or by simply expressing the desire to never go to jail again.

For example, the next time that Foster was in treatment, he describes how pressures associated with opioids illegality–such as the need to steal in order to support his habit and the consequences that could result—pushed him toward MMT.

> David: So the second time that you got on the clinic, that was not court mandated?
>
> Foster: No, no, [I got on MMT that time] cause I was waking up sick too much, and you know, I didn't want to steal to support my habit. You know that we have to do things to support our habit. So I was on verge of saying, you know what, I'm going to stop myself before someone stops me. (Foster, 2014)

Thus, despite technically entering MMT on his own accord, Foster described his decision as constrained by a framework of structural risks due both to the illegality of opioids themselves, and the need to engage in illegal activities to generate enough funds to purchase them.

Moreover, some participants' responses suggested that their decision to attend MMT was related to their desire to obtain opioids without the hassles, risks, and legal problems associated with criminalization rather than an attempt to "treat their addiction" or become "abstinent." For example, Allison described how the constant cycle of craving and withdrawal–an everyday experience for many people that use illegal opioids–prevented her from living a "normal" life. As she describes.

> And so, I didn't want to crave it anymore. And when I found methadone, my thing is I wanted maintenance. I did not want to detox anymore. I just don't want to crave, because I know for me to detox is not the answer. The whole idea was to stop craving ... so that I would have energy to lead a normal life. Because fighting the crave took too much energy out of my day . . . Too much energy. I don't want to fight a crave anymore, and I found that methadone completely alleviates the crave, the thought of it, the desire for it or anything. It just it really limits the crave and for me to detox and be clean there's always going to be a little bit ... (Allison, 2014)

Thus, in contrast to the dominant institutional narrative that imagines all patients attend MMT as a means of seeking treatment for their addiction, our data shows that for many, it is the access to safe, regulated, and legal opioids that MMT provides which drives many patients there.

Peer and Family Pressure

Participants also described substantial pressure associated with their relationships with friends and family. Research demonstrates the importance of family and the desire to please them, especially those from marginalized and/or stigmatized populations, in peoples' choices (Elizur and Ziv, 2001; Paul and Nadkarni, 2017). This sometimes manifested not only in a desire to please people they loved, but also through the complexities of trying to manage a family and related responsibilities while also managing one's physical dependence to opioids.

For example, in addition to the legal issues she explains, Monica also describes trying to manage related family problems, that were exacerbated by the consequences of her substance use. She states:

> "Yeah. So within, I would say, eight months or so or using, I lost my job, because I was a medical assistant for 16 years and I stole copays because the money was, I needed it because I had five kids and my full time job is paying that, they're in hockey, Catholic school, everything. . .
>
> So, I had to support my habit. Where was I? So within that eight month period of starting, I lost my kids, my house. My example husband kicked me out, he's like, "Get out, you're done," or whatever. You know, technically I still have custody of them but they live with him. That's a whole other. And so all of that happening just made my use get worse. . .
>
> I spiraled. My parents don't talk to me, don't talk to us. You're done. And I was like, this whole unconditional love thing, you're always here for each other . . . And it was like, I didn't get the memo. "We're always here for you, but if you become a drug addict, that's it." So, losing my kids, my parents, my family, it just made it more out of control. And then of course now with no job to support my habit, you start stealing, and that's where the petty larcenies and stuff came in. *So basically, I was forced into an outpatient. And then afterwards, when I'm in the outpatient they're like, I said, "I'm thinking about going to methadone."* (Monica, 2014)

Like many people who use illegal drugs, Monica's difficulties were exacerbated when her family, who perceived Monica's problems as caused by her poor individual choices, gave up and began to distance themselves from her. As a result, she felt that she had no other choice but to attend treatment.

The approval of family members and friends also exerted a strong influence on participants' decision-making regarding treatment. For example, Charles, a white man in his late twenties, described himself as completely unwilling to attend treatment until his girlfriend's overdose and death led to a dialogue with his father that resulted in his acceptance him of his parents' desire for him to attend treatment. He states:

> Charles: About 5 days later [after the overdose death of his girlfriend], I was sitting drinking Heinekens with my dad watching a soccer game, a European soccer game. My mom was at work and I said to him, I said to my dad, I said, "Dad, I've been looking at these methadone clinics, and I think I need to go to one. Can you take me to one after the game?" And he said, "Yeah, I'll take you." He's like, "Your mom's going to fucking kill me, though." I said, "Yeah, yeah, I know. I know she's going to fucking kill you"
>
> David: Because of what? Because she had bad feelings about methadone?
>
> Charles: No, no, because I admitted to them that I had been using heroin for the last 2 weeks, and at that point, I was kind of hooked again.

Thus, family exerted influence over participants both as a coercive force that pressured some participants into treatment, but also through an internalized desire on some to please their family friends by making choices they would approve of.

Fear of Losing One's Children

The threat of state intervention, and particularly the potential of Child Protective Services (CPS) to remove children, was a strong motivator for participants, especially women, with children. CPS has extensive powers to make demands over parents they believe to be unfit—particularly when drug use is involved (Johnson and Sullivan, 2008; Choate and Engstrom, 2014). As the following participant describes:

> Monica: I went with the National Association of Pregnant Women to the convention in Tennessee—it revolved around pregnancy, drug use, and motherhood. Because they have that law where [if you're using illegal opioids] they charge you with a felony, I think it's called the Fetal Assault Law, they're hoping to change it in July . . . Because what they're finding is women crossing state lines to give birth; women not getting prenatal care. There was one women she wasn't wearing her seatbelt and she saw the cop was gonna pull her over and she just sped away because she knew she was done, she had a warrant, and she was just like, "They're taking your child away." Even being on methadone, they consider that being on drugs. And then when you hear the Obstetricians and all these professionals talking [about], you know, being on opioids, or being on methadone, is not as harmful to the fetus, a Xanax, and anti-depressants too." (Monica, 2014)

As Monica explains, women who are pregnant and use opioids may have their children taken away due to the Tennessee Fetal Assault law which research confirms did lead to an increase in out-of-state births particularly among racial and ethnic minorities (Choi and Leslie, 2020). However, she was surprised when she went to a medical conference and discovered that methadone, anti-anxiety medications, and anti-depressants are all safe to use when pregnant. Despite the science, Monica and others faced real consequences if they used drugs.

The fear of ones' children being taken away not only affected peoples' choice to attend treatment but also factored into their choice of which kind of treatment to attend. Specifically, participants sought out treatment models that would model appear more impressive to agencies with the ability to exercise power over their families. Sometimes this meant that women would get off methadone and opt for a less stigmatized drug such as buprenorphine, which they could acquire at a pharmacy once a month.

For example, one participant chose buprenorphine despite her preference for methadone, with disastrous results. Jenny, a 45-year old (at the time of the interview), white women with two children, one of them, a young girl with special needs and significant health issues, stated not only that she preferred methadone because of its greater pharmacological effect toward reducing cravings, but also that she believed it to be better researched and thus felt more comfortable using it, particularly after the birth of her daughter.

> "The only time I was on methadone maintenance was, it started when I first found out that I was pregnant with Sandra, I had been on Suboxone, yeah, the Subutex maintenance for a long time, But when Dawn was born with a heart defect and then she had just been diagnosed with autism, at that time my thought was that methadone had a lot more research, and I actually didn't really have a doctor. So my thought at the time was the best thing to do was go be under their care because I knew after Sandra was born, I knew I was going to have to deal with CPS and all that stuff because I've had to with all my kids. But my main thing was safety, I knew that there was research on the methadone, so that was my motivation to switch to the methadone." (Jenny, 2014)

However, during the pregnancy and birth of her second child, Jenny experienced significant harassment and abuse by medical professionals over her use of MMT. As she describes:

> "I was told by that lady [the nurse], "how dare you give that baby that milk," after the doctor had just been like "please pump milk and give it to the baby." [She went on saying] "How dare you give that to your baby? Why are you on such a high dose of methadone?." I said that I didn't realize I was on a high or low dose—I was on the dose that the doctor gave me. So, long story short, because this story still makes me sick to my stomach, they got to the point because I was on methadone, even though I was in a program, they had this emergency meeting where they were gonna remove Dawn and Sandra from my care." (Jenny, 2014)

Jenny was able to avoid losing her children, which she believes was only because she and her husband had retained their own therapist, outside of the court system, who was able to speak on their behalf. However, the experience had badly shaken both parents, and she decided to switch to buprenorphine, a similar, though much less stigmatized medication which can be obtained at a pharmacy rather than a methadone clinic. She emphatically stated:

> "When I think of how close I came. And the things that these CPS workers, who are supposed to be educated. And the way the nurses treated me . . . " (Jenny, 2014)

Unfortunately, since buprenorphine is a partial agonist compared to methadone, a full agonist, as she suspected, it did not prevent cravings as well, and she eventually began injecting to increase its euphoric/therapeutic value. Since she viewed her actions as her own "poor choices" rather than the result of structural and institutional policies, she hid this practice from family, friends, and her doctor. After a few years, the injection site became infected and grew increasingly worse as she continued to inject there. Eventually, she was rushed to the hospital with a dangerously high fever and rapidly deteriorated, falling into a comatose state. A week later she had died from complications associated with clotting and infection of the injection site.

Internalized Stigma and Societal Stigma

Not surprisingly, stigma against people who use illegal opioids also motivated some participants to use MMT. For example, participants stated that they went into treatment because they didn't want to remain a "Dopehead" or "fuck-up" any longer. In contrast, when participants where on treatment they referred to themselves as "clean." By far, this was the most prominent way that self-stigma, also referred to as internalized stigma, manifested.

Many also reported feeling self-conscious about how they looked and were perceived by others. Participants reported feeling as though others perceived them as dirty or mistrust worthy. For example, one participant, a white man in his late twenties stated:

> "Back when I was using, I looked like a piece of shit. I mean, I could't even walk into a regular store without a cashier being like, "Oh, here's a fucking junkie." And that was, I'll say, after I got off it, I'd been clean about 76 days, going back, I was like, "I don't want to look like that again. I don't want to have myself perceived like that again." (Charles, 2014)

Although this is complicated by the fact that MMT is also stigmatized, since methadone is legal, it is far easier to hide and manage compared to heroin which must be obtained through illicit and unreliable sources often multiple times a day. As such, participants perceived MMT to be the better option because it was legal and less stigmatizing than illicit drug use. Yet, oftentimes, they could not quite shake the stigma, which manifested as internalized stigma.

In line with this view, Foster did not conceptualize his use of MMT through narratives of treatment of recovery but saw it as a way of dealing with the contextual realities of illegal substance use. For example, the following conversation demonstrates this:

> David: Okay. Do you consider yourself as being in recovery now? Now that you're on methadone?
>
> Foster: No.
>
> David Frank: No. Tell me why.
>
> Foster: Because I know deep down I'm not really *clean*. . ..I'm just doing something to maintain.

Here Foster uses the language of "clean" to describe someone who does not use drugs and delineate such individuals from himself. In line with many 12 step programs ideologies, methadone is indeed considered a drug, and therefore someone using it is not drug free, or in Foster's words "clean." Ideas such as this were prominent among participants in this study.

DISCUSSION

This article examines if, and how, OST patients' descriptions of treatment uptake evince larger forms of constraint. Findings demonstrate that patients' treatment decisions are often made within a context of constraint that limits their agency. Similarly, narratives that position OST patients' treatment decisions as strictly volitional ignore the role of larger, structural forces in the lives of people who use drugs. Instead, we argue for an approach to understanding peoples' treatment decisions that better reflects MMT's position within complex, external, and often oppressive, structural contexts that drive people who use illegal drugs to treatment.

Although the decision to enter substance use treatment, or a particular type of substance use treatment, is typically conceptualized as an unconstrained action, like all social phenomenon, it is the result of a complex interaction between individual and structural forces (Mills, 2000). These forces are not discrete but rather interact with, and reinforce each other, pushing people who use drugs into particular treatment decisions. Our data demonstrates that in contrast to the institutionally dominant view which describes treatment in purely volitional terms, external forces, experienced as coercive, played a substantial role in participants' treatment choices. In particular, participants experienced pressure related to: 1. A feeling of limited choices due to drugs' illegality; 2. Peer and family pressure; 3. Fear of losing children; and 4. Internalized and societal stigma (i.e. feeling they are dirty or bad for using). However, within situations of constrained choice participants often still found ways to assert their agency. For example, those who were able to use MMT to their benefit, especially as a strategy to avoid incarceration.

All of the themes that emerged were directly influenced by larger structural forces that were out of the control of participants, mainly the illegality of drug use which carried with it the threat of incarceration and/or losing one's children. Policies criminalizing drugs likely not only affect individual choices, such as choosing between treatment or incarceration, but also affect family and friends perceptions of drug use and well as one's perception of self (i.e., internalized stigma). Further, people who use drugs do not live in isolation, they have family and social networks whom they care about, and whom they would like to please and keep in their lives. Thus, the consequences of criminalizing drugs influenced treatment decisions for participants, not only directly to avoid criminalization, but also to please family and friends and to gain a better self-worth (though not always achieved completely).

Therefore, narratives that position peoples' treatment choices as purely volitional are problematic, firstly, because they misrepresent the needs of PWUD. As Frank has argued previously, if treatment is conceptualized individually, without acknowledging its role as a refuge from criminalization, it is likely to embrace a punitive model in-line with that discourse's focus on the need for individual change (Frank, 2018). Moreover, such policies provide political cover to policies that criminalize PWUD. By framing peoples' decisions to enter treatment as unconstrained, individually based choices, the coercive harm created by policies like criminalization and the War on Drugs, in the lives of PWUD is erased in favor of a narrative based strictly on sick/bad people choosing to "get better."

This analysis aligns with the work of a growing body of multi-disciplinary research that is critical of the nearly universal use of "addiction" to understand substance use and treatment (Frank, 2018; Fraser et al., 2014; Campbell, 2012). Although addiction-as-disease models still dominate both in scholarly and lay settings (Volkow and Fowler, 2000; Volkow et al., 2016), scholars have been increasingly critical of its lack of conceptual clarity and rigor and focus solely on the individual as an agent of harm (Keane, 2002; Reinarman, 2005; Davies, 2013; Fraser et al., 2014). For example, social scientists, like Suzanne Fraser and Nancy Campbell, have questioned how well-suited the concept of addiction is to understand Medication assisted Treatment (MAT) (Fraser and Valentine, 2008; Campbell, 2011). Similarly, Rebecca Tiger's work on Drug Courts demonstrates that such interventions, which are based on an addiction-as-disease view of substance use, can cause more problems than they solve (2013).

It also aligns with the many critiques of MMT as being overly punitive. For example, researchers have pointed out problems with MMT's restrictive take-home policies, intrusive use of drug testing, and a power differential between patient and provider that almost certainly contributes to low rate of use and retention (Frank, 2020; Strike and Rufo, 2010; Damon et al., 2017; Pani and Pirastu, 2000). Evincing this, low-threshold clinics, that aim to reduce such barriers, demonstrate better rates of patient retention and satisfaction as well as reducing harms such as overdose mortality and all-cause mortality (Nolan et al., 2015; Strike et al., 2013;

It is important to point out that this analysis focuses specifically on MMT, a treatment model whereby patients remain using opioids. While the authors believe that criminalization and the War on Drugs exert pressure on PWUD to enter all forms of treatment, it is likely to be strongest in Opioid Substitution Treatment models, like MMT, because of this fact.

There are several limitations to this research. Firstly, that one of the two authors is on MMT could be considered a source of bias (the other author is not, which could also be considered a bias). However, research using Marxist, feminist, and other post-structuralist-inspired theoretical methods such as CDA, often accept that all positionality is biased, and distinctions made within scholarly work between bias and objective or insider vs. outsider are artificial (Fairclough and Wodak, 1997; Fairclough, 2013). Yet, we do not think that such distinctions are meaningless toward an interpretation of our data, and thus, we are being transparent about Frank's use of both illegal heroin and MMT. Similarly, as this study is not based on a representative sample, results cannot be generalized to a larger population of PWUD. Moreover, we were also unable to collect accurate demographic information for all of the study participants, partially because many of the interviews began informally, through conversation. Additionally, since this research was conducted in New York City participants likely had better access to MMT than in less urban geographic areas. Research has demonstrated the dearth of services for people who use illegal drugs in non-urban settings (Jones, 2018; Cochran et al., 2019). Similarly, because of the clustering of harm reduction services in urban locations, participation in MMT is probably less stigmatizing than in other settings. In light of that, results may not be transferable to less urban locations. However, we could potentially conclude that PWUD in less urban parts of the US likely experience even more coercion and negative consequences for using substances.

Nevertheless, this research has important implications for how drug treatment is conceptualized and administered.

We argue that narratives which conceptualize individuals' decision to attend treatment as strictly a matter of individual choice are reductive and problematic by ignoring the tremendous socio-political pressures, primarily due to drugs' illegality, and related problems, on peoples' decisions regarding substance use treatment. Rather, the analysis of such decisions should be broadened to include an understanding of how larger structural forces—notably criminalization and the War on Drugs—constrain the agency of people who use illegal drugs in all of their decisions, but especially those related to treatment. Yet importantly, they do not mute the agency of people using drugs, and many people find ways within incredibly constrained conditions to navigate their trajectories as they feel is most beneficial for them (Koester et al., 1999; Mateu-Gelabert et al., 2010; Harris and Rhodes, 2013). Acknowledging the interplay between individual and structural forces in the treatment decisions of criminalized drug users, and how a person's agency is constrained due to these forces, will not only provide a more sophisticated and evidence-based understanding of PWUD's motivations, but can also provide a more productive platform from which to identify criminalization and the War on Drugs as forces of harm in the lives of people using illegal drugs. Moreover, it may pave the way for new approaches to treatment so that we can meet the United States goals of providing substance use treatment to a greater number of people (Healthy people, 2020).

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by The CUNY Graduate Center Internal Review Board. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

The data collection was completed entirely by Frank. Both authors worked collaboratively on developing a theme based on that data. Frank wrote the initial rough draft of the paper and from that point, both authors collaboratively developed the paper towards its final form.

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A Multistage Process Model of How a Person Who Currently Injects Drugs Comes to Assist Persons Who Do not Inject with Their First Injections

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Injecting drugs for the first time almost always requires assistance from an experienced person who injects drugs (PWID). While there has been moderate amount of research on PWID who assist with first injections, most of this research has focused on identifying characteristics of PWID who assist with first injections. We do not have a formal model that describes how the minority of PWID come to assist do so, while the majority never assist. Through comparison of persons who did or did not recently assist with first injections using data from PWID in Tallinn, Estonia (N = 286) and Staten Island, New York City (N = 101), we developed a formal multi-stage model of how PWID come to assist with first injections. The model had a primary pathway 1) of engaging in “injection promoting” behaviors, 2) being asked to assist, and 3) assisting. Statistical testing using odds ratios showed participation in each stage was strongly associated with participation in the next stage (all odds ratios >3.0) and the probabilities of assisting significantly increased with participation in the successive stages. We then used the model to compare engagement in the stages pre-vs. post participation in an intervention, and to compare persons who recently assisted to persons who had assisted in the past but had not recently assisted and to persons who had never assisted. Advantages of a formal model for how current PWID come to assist with first injections include: facilitating comparisons across different PWID populations and assessing strengths and limitations of interventions to reduce assisting with first injections.

Keywords: persons who inject drugs (PWID), Estonia, Staten island, non injection drug use, New York City

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INTRODUCTION

The transition from non-injecting to injecting drug use greatly increases the likelihood of both individual and societal adverse consequences of illicit drug use. Compared to non-injecting use, injecting is more likely to lead to blood-borne virus transmission (HIV, hepatitis B and C), abscesses and other bacterial infections, fatal overdoses, and more rapid development of substance use disorders (Mathias, 1991; Griffiths et al., 1994; McBride et al., 2001; Mateu-Gelabert et al., 2005; Ochoa et al., 2005; Simmonds and Coomber, 2009).

The transmission of HIV through multi-person use (sharing) of needles and syringes for drug injecting deserves additional comment. During the 1980s, 1990s and 2000s HIV epidemics with seroprevalence reaching 30% or higher occurred in many parts of North America, Europe and Asia (Des Jarlais et al., 1994; van den Hoek et al., 1988; Wiessing et al., 2008). The development and implementation of "combined prevention and care for PWID" (primarily syringe service programs, opiate substitution treatment (OST) programs, and antiretroviral treatment as prevention) have led to "ending" many high prevalence HIV epidemics in North America and Europe (D.C. Des Jarlais et al., 2016). Despite these successes of combined prevention and care for PWID, multiple new outbreaks of HIV among PWID have occurred in the last decade. Outbreaks have occurred in Europe, Israel, Taiwan, and the US (Des Jarlais et al., 2020; Huang et al., 2019). Even with the highly effective tools of combined prevention and care, injecting drug use must be seen as a continuing threat for further transmission of HIV.

Injecting an illicit drug is a complicated and potentially dangerous procedure, and almost everyone who begins injecting requires the assistance of an experienced injector for a first injection (Rhodes et al., 2011; Kolla et al., 2015). We do have a relatively good understanding of the social-cognitive and interpersonal processes through which persons who use but do not inject drugs (non-PWID) are initiated into injecting (Rhodes et al., 2011; Kolla et al., 2015; Wenger, Lopez, Kral, and Bluthenthal, 2016; Guise, Horyniak, Melo, McNeil, and Werb, 2017). First, through their participation in the general illicit drug use subculture and their interactions with persons who inject drugs (PWID), non-PWID "normalize" injecting as a route of drug administration. Second, through further discussions with PWID and possible observations of PWID actually injecting, they become more interested in injecting, become motivated to try injecting, and then ask for assistance with their first injection.

We do not have a comparable process model for how some PWID come to provide assistance with first injections. Multiple cross-sectional quantitative studies of PWID who have provided assistance with first injections have found that only a minority, typically 10%–30% of PWID, have ever provided assistance with first injections (Crofts, 1996; Hunt et al., 1998; Bryant and Treloar, 2008; Rhodes et al., 2011; Bluthenthal et al., 2014; Rotondi et al., 2014). These quantitative studies have also identified a wide variety of factors that differentiated between PWID who assisted with first injections vs. PWID who did not assist with first injections, including: gender, age, race/ethnicity, educational attainment, frequency of heroin injection, and use of non-injectable drugs, (see Barnes et al., 2018) for a review.

Overall this is a long list of disparate factors. Some of the differences in the factors identified as distinguish between PWID who assisted vs. PWID who did not assist undoubtedly arise from methodological differences—different questionnaires, different time frames for having assisted—and some of the differences may arise from conducting the studies in different PWID populations. Nevertheless, given the common processes that underlie how non-PWID come to engage in first injections and the near universality of PWID receiving assistance with their first injections, one would expect that there may also be common process that lead current PWID to assist with first injections.

A formal conceptual description of how this minority of PWID come to provide assistance with first injections would permit statistical assessment of the fit of the model in different PWID populations and comparisons of the processes in the different populations. Formal specification of such a model should also provide insight into potential interventions to reduce the likelihood that current PWID would assist with first injections. Interventions that would reduce the likelihood of current PWID assisting with first injections could be extremely useful in reducing many of the adverse consequences of illicit drug use, including HIV and HCV transmission, overdoses, and bacterial infections (Werb et al., 2018).

We report here on the development of a multi-stage social process model for how some PWID came to recently assist with first injections while the great majority did not recently assist with first injections. We then apply the model to compare engagement in the different stages pre-vs. post participation in an intervention to reduce assisting with first injections, and then to differentiate between PWID who have never assisted with a first injection vs. those who did not recently assist but have assisted in the past. A final analysis identified characteristics of PWID who assisted with only one first injections and then did not assist with any other first injections.

The data used in developing the model come from the baseline (pre-intervention) data in a two-site clinical trial of an updated version of the "Break the Cycle" intervention (Des Jarlais, 2018; Des Jarlais et al., 2019).

METHODS

Generating a Multi-Stage Process Model for Assisting with First Injections

Our model development was informed by review of the qualitative and quantitative literature on PWID assisting with first injections (Rhodes et al., 2011; Kolla et al., 2015; Wenger et al., 2016) and our previous research with persons who use drugs (both PWID and non-PWID). We also conducted qualitative research specifically to better understand why many PWID do not assist non-PWID with first injections (Barnes et al., 2018).

The led us to formulate requirements for a quantitative model that would describe how a few current PWID come to assist with a first injection and how the great majority of PWID do not assist with first injections:

1. The model would need to be consistent with the qualitative research on how PWID come to assist with first injections and with the qualitative and quantitative research on how non-injecting drug users come to inject for the first time.
2. Assisting with a first injection would not be a single, spontaneous event but rather the result of a multi-stage process of interactions between PWID and non-injecting drug users.
3. Engaging in each stage would be positively associated with engaging in the next stage and engaging in each successive stage would be associated with an increasing probability that a current PWID would assist with first injections.
4. Engaging in "injection promoting behaviors" (talking positively about injecting to non-injectors, injecting in front

of non-injectors, and offering to assist with a first injection) would be a critical early stage in the process.
5. Assisting with a first injection is a consensual act, requiring explicit agreement between the PWID who provides assistance and the non-PWID who receives assistance.

We applied these requirements to the baseline data from participants in a two-site clinical trial of an updated version of the Break the Cycle intervention (Uusküla et al., 2018). Break the Cycle is an intervention based in social cognitive theory and motivational interviewing to reduce the likelihood that a current PWID will assist a non-PWID with a first injection. It was originally developed by Hunt et al., 1998 and later adapted by Strike et al., 2014 to use peers as the interventionists. The Hunt intervention consisted of questions in five different sections: the participant's own initiation, their initiation of others, the risk from initiation for themselves and the initiate, identification of aspects of their own behavior that may inadvertently promote injecting, and generation and rehearsal of responses to a series of vignettes describing common initiation scenarios. Strike extended the intervention to include information on safe injection education and sources of syringes and injection equipment in the community, which was developed from the Canadian AIDS Treatment Information Exchange (Canadian AIDS Treatment Information Exchange, 2008).

Clinical Trial Study

The full results of this clinical trial have been reported elsewhere (NCT 03502525) (Des Jarlais, 2018; Des Jarlais et al., 2019) so that only a brief description will be presented here.

Participant Eligibility

PWID were eligible for the study if they were 18 or older, spoke Estonian or Russian (Tallinn) or English (Staten Island), reported having injected in the previous two months, and were able and willing to provide informed consent.

Recruitment

Tallinn

Respondent driven sampling (RDS) (Heckathorn, 1997; Heckathorn, 2002) was used. The syringe exchange program Convictus served as the research site. After study participation, subjects were provided coupons for recruiting up to three peers to participate in the study.

New York City

Program staff on the Community Health Action of Staten Island (CHASI) mobile syringe exchange bus were made familiar with the eligibility criteria and referred potentially eligible participants to research staff on the unit based on a convenience sampling approach. Research staff screened the referrals.

Study Procedures

After eligibility determination and informed consent, participants completed a face-to-face interviewer-administered structured questionnaire which lasted approximately 30 min. Questions elicited information on demographics, experiences with injection and other drug use, sexual risk behavior and use of various HIV/harm reduction-related services. The behavioral questions used a "in the past 6 months" time framework.

Intervention

Immediately after the baseline interview, the PWID participated in a "Break the Cycle" intervention conducted by the interviewer, who had been trained in the intervention (Des Jarlais et al., 2019). The intervention session took 30–40 min. The intervention was aimed at enhancing current injectors' motivation and skills to avoid helping non-injecting drug users transition to injection drug use. It was informed by two main approaches to behavior change: Social Cognitive Theory, which explains behavior change as the result of peer modeling, expectancies about the target behavior, and perceived self-efficacy to carry out the target behavior (Bandura, 1993); and Motivational Interviewing (MI) (Miller and Rollnick, 2012). MI is a client-centered approach that proceeds from the premise that almost all individuals have ambivalence about behavior change. MI is aimed at articulating and resolving that ambivalence in the direction of healthier behavior and pinpointing next action steps.

The intervention had seven main parts: 1) discussion of own first time injecting drugs; 2) discussion of injection "promoting" and "assisting" behaviors, and experiences with and attitudes toward these behaviors; 3) discussion of the health, legal, social, and emotional risks of injection (including a module on safe injection practices); 4) role-plays of behaviors and scripts for avoiding or refusing requests to help non-PWID inject for the first time; 5) role-plays of talking with other PWID about not encouraging non-PWID to start injecting; 6) discussion of coaching non-PWID in safer injection practices, should they feel helping is their best option; and 7) discussion of how naloxone can be used to reverse overdose.

Measuring "Injection Promoting" and "Assisting with a First Injection" Behaviors

We developed and pre-tested specific question about attitudes and behaviors related to assisting with first injections. These questions included:

1. Engaging in "injection promoting" behaviors, defined as: 1) speaking positively about injecting to non-PWID, 2) injecting in front of non-PWID, and 3) offering to give a first injection. Separate questions were asked about each of these distinct behaviors.
2. Whether the participant had "assisted with a first injection," defined as "explaining, or describing or demonstrating how to inject to a person who then injected for their first time," or "injecting a person who had not injected before." This was asked as a single question as our pre-testing indicated that many of these behaviors were performed within a single episode of assisting.

We asked questions on assisting both at the baseline interview and at the follow-up interview, which occurred approximately six months after the initial interview was conducted. Follow-up

TABLE 1 | Demographics, drug use characteristics, and promoting behaviors among PWID in Tallinn and Staten Island, New York City.

	Tallinn		**New York city**	
	N	**%**	**N**	**%**
Total	286	100	101	100
Avg. age (SD)	33 (7)	—	44 (11)	—
Avg. years injecting (SD)	14 (6)	—	17 (14)	—
Gender				
Male	221	77	63	62
Female	65	23	38	38
Race or ethnicity				
Russian	230	80	—	—
Estonian	39	14	—	—
White	—	—	51	51
Black	—	—	22	22
Latinx	—	—	13	13
Other	17	6	15	15
Non-injecting drug use				
Any non-injected drug use	193	67	94	93
Speedball sniff/snort/smoked	—	—	46	46
Heroin sniff/snort/smoked	—	—	57	56
Fentanyl sniff/snort/smoked	99	35	4	4
Opiate analgesic pills swallowed	44	15	53	52
Cocaine sniff/snorted	—	—	41	41
Crack smoked	—	—	71	70
Amphetamines	43	15	19	19
Street methadone	28	10	33	33
Injecting drug use				
Heroin injected	—	—	96	95
Speedball injected	—	—	38	38
Cocaine injected	1	1	36	36
Fentanyl injected	205	72	4	4
Opiate analgesics injected	3	1	14	14
Amphetamines injected	185	65	—	—
Receptive sharing	40	14	9	9
Distributive sharing	67	23	9	9
Sexually active	242	85	79	79
Unsafe sex	178	74	25	25
Friends assisted w/1st injection	84	29	53	53
Likely to assist w/1st injection	67	36	14	14
Any promoting behavior[a]	81	28	38	38
Talked positively about injecting	20	7	25	25
Modeled injecting	74	26	25	25
Offered to inject	3	1	5	5
Helped inject last 6 months	12	4	12	12

[a]*Talking, modeling, offering to inject.*

interview questions queried specifically on behaviors in the last six months (i.e. the period between the baseline interview/intervention and the follow-up interview only).

RDS Weighting

For Tallinn, there were small difference between the RDS weighted and unweighted values (<3% for all major variables). We therefore used the unweighted data to facilitate comparisons with Staten Island.

Missing and Inconsistent Data

Thirteen subjects from Tallinn and 2 subjects from Staten Island with missing or inconsistent data on injection promoting, being asked to assist, and assisting with first injections were excluded from the analyses.

Honoraria

Participants were paid modest honoraria for their time and effort in the study, and in Tallinn, for recruiting additional participants.

Audiotaping of Intervention Sessions

In order to monitor fidelity of the interventions and to obtain greater insight into how participants experienced the intervention, we audiotaped the intervention sessions. This was done with explicit approval of the participants, and they were cautioned not to use the names of any other persons they mentioned during the intervention sessions.

Ethical Approval

Ethical approval for the study was obtained from the Ethics Review Board of the University of Tartu, Estonia and from Mount Sinai Beth Israel Medical Center and New York University School of Medicine Institutional Review Board in New York, United States.

RESULTS

Demographics, Drug Use, and Factors Associated with Injection Promoting Behaviors

Table 1 presents demographic characteristics, drug use, and injection initiation related behaviors for the pre-intervention interviews of the participants used in developing the multi-stage model. The drug use related behaviors referred to the 6-month period prior to the interview. A total of 286 PWID were included from Tallinn and 101 were included from Staten Island.

There are major differences between the Staten Island and the Tallinn subjects in almost all of the injecting and non-injecting drug use variables, to where standard statistical testing is not meaningful. The two samples clearly come from different drug using populations. Majorities of participants in both sites used non-injected drugs and thus were likely to have opportunities interact with non-PWID.

Engaging in "Injection Promoting Behaviors"

Substantial percentages of the participants reported engaging in at least one "injection promoting" behavior in both sites—28% (81/286) in Tallinn and 38% (40/101) in Staten Island. We tested all factors (except assisting with a first injection) in **Table 1** for associations with engaging in any promoting behavior. **Table 2** shows factors that were significant in either or both of the two samples. It should be noted that "any non-injecting drug use" was strongly associated with engaging in promoting behavior for the Tallinn sample. "Any non-injecting drug use" was not statistically associated with promoting behavior in the Staten Island sample because almost all (94%) of the Staten Island participants reported non-injecting drug use. Thus, non-injecting drug use among the Staten Island participants did not distinguish engaging

TABLE 2 | Factors significantly associated with injection promoting behavior[a] among PWID in Tallinn and Staten Island, New York City.

Site	Staten Island, New York city			Tallinn Estonia		
Variable	**OR**	**95% CI**		**OR**	**95% CI**	
Age (continuous)				0.94	0.90	0.98
Gender						
Male (female: ref)	3.41	1.35	8.58			
Race/ethnicity						
Black (white: ref)	0.29	0.09	0.99			
Non-injection drug use						
Any non-injection drug use				2.61	1.44	4.97
Street methadone use	3.50	1.47	8.36			
Injection drug use						
Less frequent drug injection				1.79	1.01	3.13
Larger injection network size[b]	1.03	1.00	1.05	1.02	1.01	1.03
Receptive sharing	16.53	1.98	138.30	2.84	1.43	5.65
Distributive sharing	6.89	1.35	35.15	3.48	1.97	6.21
Friends who assisted w/1st injection	2.89	1.24	6.74	5.11	2.60	10.34
Endorsing likely to assist with first injection in future	5.27	1.52	18.27	2.85	1.65	4.94

[a] *Promoting behavior–talking positively about, demonstrating, offering to help with injecting.*

[b] *Injection network size was categorized as "larger injection network size" when network size was greater than the median (7).*

from not engaging in promoting behavior but should not be ruled out from being involved in promoting behavior. We considered these as "factors associated" with promoting injection but note that many of them were likely to be present before a PWID engaged in promoting behaviors, and thus may have served as causes for engaging in promoting.

There were both similarities and differences in the "factors associated with injection promoting" across the two sites. The differences may reflect how variations in the local drug use culture feed into a common predominant pathway to assisting with first injections.

Across the two sites, the best predictor of which PWID engaged in promoting behavior was whether they exhibited 4 or more of these factors. In New York, 29/55 (53%) of the PWID who endorsed 4 or more factors promoted vs. 9/46 (20%) of the PWID who endorsed less than 4 factors (chi square = 11.7, $p = 0.001$). In Tallinn, 23/37 (63%) of PWID who endorsed 4 or more factors promoted vs. 53/236 (23%) of PWID who endorsed less than 4 factors (chi square = 24.3, $p < 0.001$). The odds ratios between having 4+ "associated factors" and engaging in injection promoting were in Tallinn (OR = 7.3, 95% CI 3.3–16.4) and Staten Island (OR = 4.6, 95% CI 1.9–11.3).

Being Asked to Assist with a First Injection

Engaging in injection promoting behavior was strongly associated with being asked by non-PWID to assist with a first injection during the 6 months prior to the interview. In Staten Island, 24/38 (63%) who had promoted were asked by a non-PWID to assist with a first injection vs. 21/63 (33%) who had not promoted. In Tallinn, 31/86 (36%) of the PWID who had promoted were asked to assist vs. 28/202 (14%) who had not promoted. Both of these relationships between engaging in injection promoting and being asked to assist were substantial and statistically significant in Tallinn (OR = 3.5, 95% CI 1.8–6.6) and Staten Island (OR = 3.4, 95% CI 1.5–8.0).

Assisting with a First Injection

Being asked to assist was strongly associated with actually assisting with a first injection; 21% (12/58) participants in Tallinn who were asked to assist assisted with a first injection and 27% (12/45) in Staten Island who were asked assisted. In neither site were there any participants who assisted who had not been asked to assist, so that ORs could not be calculated for assisting with being asked vs. assisting without being asked.

Whether participants who were asked to assist had engaged in injection promoting behavior in the 6 months prior to the interview was strongly associated with whether they assisted. In Tallinn, 10/30 of those who promoted and were asked did assist vs. 2/28 of those who did not promote and were asked (OR = 6.5, 95% CI 1.2–65.6). In Staten Island, 10/24 of those who promoted and were asked assisted vs. 2/21 of those who did not promote and were asked (OR = 6.8, 95% CI 1.1–70.3).

Flow Diagrams and Probabilities of Assisting with a First Injection

Figure 1 shows flow diagrams of the different stages leading from engaging in injection promoting behaviors to actually assisting with a first injection at each site. In both sites there was a predominant pathway (engaging in injection promoting behavior and then being asked to assist with first injection, noted in red) and a secondary pathway (not engaging in promoting behavior but being asked to assist, noted in black) leading up to actually assisting with a first injection.

As specified in the development of the model, engaging in additional stages (injection promoting behavior, being asked to assist) was associated with increases in the probability of assisting with first injections.

For Tallinn

1. Participants who engaged in neither promoting nor being asked had a 0 (0/174) probability of assisting.

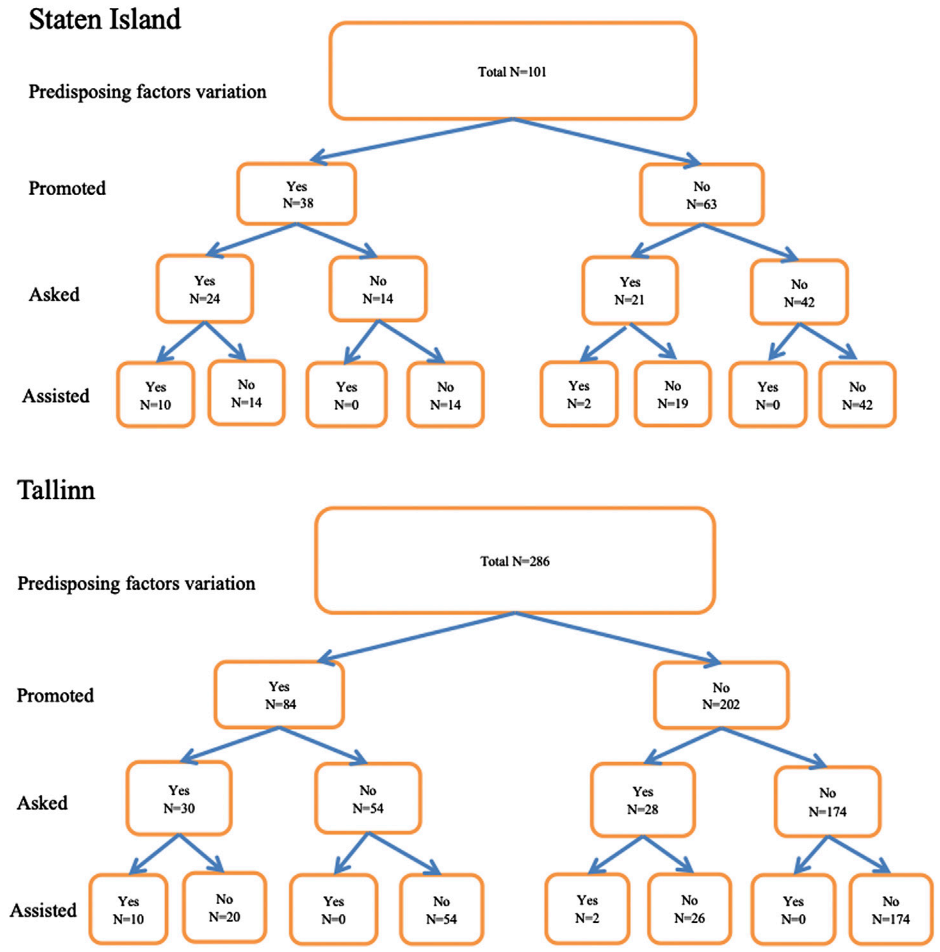

FIGURE 1 | Flow diagrams of the different stages leading from engaging in injection promoting behaviors to actually assisting with a first injection at each site.

2. Participants who engaged in promoting had a 0.12 (10/84) probability of assisting.
3. Participants who both engaged in injection promoting and were asked to assist had a 0.33 (10/30) probability of assisting.

For Staten Island

1. Participants who engaged in neither promoting nor being asked had a 0 (0/42) probability of assisting.
2. Participants who engaged in promoting had a 0.26 (10/38) probability of assisting,
3. Participants who both engaged in injection promoting and were asked to assist had a 0.42 (10/24) probability of assisting.

For both sites, the probability of assisting greatly increased with participation in the two stages of engaging in injection promoting and being asked to assist. Fisher exact test comparisons of the probabilities of assisting given neither promoting nor being asked vs. both promoting and being asked were statistically significant, $p < 0.0001$ for both Tallinn and Staten Island.

TABLE 3 | Changes in outcomes for targeted behaviors.

	Tallinn	Tallinn[a]	Staten island	Staten island[a]
	(Pre)	(Post)	(Pre)	(Post)
	N = 230	N = 230	N = 64	N = 64
Any promoting behavior	33%	20%*	33%	28%
Asked to assist with first injection	18%	15%	44%	45%
Assisted with first injection	5%	1%*	15%	6%*

*$p < 0.05$.

[a] *Post measurement took place six months after baseline interview and intervention.*

Results II: Application of the Model to a Break the Cycle Intervention

Table 3 shows the pre-post intervention changes in the percentage of trial participants in the three stages of our multi-stage model. There was a statistically significant effect in reducing the percentage of participants who engaged in injection promoting behavior in Tallinn, but the reduction was not

TABLE 4 | Comparison of promoting behaviors and being asked to help among those who had never helped someone inject, those who had helped prior to previous 6 months, and those who in the last 6 months among PWID in Staten Island.

	Never assisted	**Assisted with first injection**	
	N = 71	**Assisted >6 months ago, N = 18**	**Assisted in last 6 months, N = 12**
Mean of facilitating factors	3.6	4.2	5.3
Median of facilitating factors	3	4	6
	(N, %)*	(N, %)*	(N, %)*
Promoted	19 (26%)	9 (50%)	10 (83%)
Were asked for assistance	25 (35%)	8 (44%)	12 (100%)

TABLE 5 | Comparison of promoting behaviors and being asked to help among those who had never helped someone inject, those who had helped prior to previous 6 months, and those who in the last 6 months among PWID in Tallinn.

	Never assisted	**Assisted with first injection**	
	N = 246	**Assisted >6 months ago, N = 40**	**Assisted in last 6 months, N = 14**
Mean of facilitating factors	3.3	4.3	4.6
Median of facilitating factors	3	4	5
Number who promoted (%)	61 (26%)	915 (38%)	11 (79%)
Number who were asked for assistance (%)	41 (15%)	6 (15%)	12 (86%)

significant in Staten Island. As noted in **Table 1**, a very high percentage (93%) of the Staten Island participants reported non-injecting use of heroin, cocaine and prescription opioids, and thus were likely to have had many opportunities to engage in injection promoting behavior with non-PWID.

There was no reduction in being asked to assist with first injections in either site. Asking to assist with first injections is largely under the control of non-PWID, so it is probably unrealistic to expect that Break the Cycle interventions would have a significant effect on being asked to assist. Different interventions that focus on non-PWID are needed to reduce asking for assistance with first injections.

There were statistically significant reductions in both sites in the primary outcome of actually assisting with first injections. We attribute this effect to the intervention focusing existing motivations to not assist and to the role play practice of declining to assist when asked to assist.

Tables 4, **5** gives a comparison of endorsing facilitating factors for injection promoting, having engaged in promoting behaviors, and having been asked to assist among those who had never helped someone inject, those who had helped prior to previous 6 months, and those in the last 6 months among PWID in Staten Island. There was a consistent pattern with the never assisters being lowest, the previous but not recent assisters being intermediate, and the recent assisters being highest on all of these measures. Substantial numbers of the never assisters, however, did engage in injection promoting behavior and had been recently asked to provide assistance with a first injection.

DISCUSSION

The postulates and stages in our multi-step process model were derived partly from the literature, and thus are not unique to this analysis. We do believe, however, that the formal statement of the model has major advantages. A formal statement permits statistical examination of the associations between participating in the successive stages and in changes in the stage-associated probabilities of assisting with first injections. The model is thus “falsifiable.” If the associations between participating in successive stages in the predominant pathway had not been statistically significant, or if the probabilities of assisting with first injection had not increased with passage through the successive stages, we would have concluded that the model did not fit the quantitative data.

The formal statement of the model and the statistical analyses then permit a close comparison across sites. The probability analyses did show very strong similarities across the Tallinn and Staten Island PWID populations. These populations clearly varied in terms of drugs injected, race/ethnicity, extent of non-injecting drug use among PWID, and the pre-intervention rates of injection promoting behavior and assisting with first injections. The similarities in the fit of the data to the model in the two sites suggest that the model may be applicable to a wide variety of PWID populations. The strong similarities across the two sites in the numbers of factors associated injection promoting across PWID who never assisted, who assisted previously but not recently, and who assisted recently suggest similarities in time (since assisting) as well as similarities across the geographic sites.

As noted in the introduction, previous cross-sectional quantitative studies of characteristics of PWID who assist with first injections noted a variety of factors, including gender, age, race/ethnicity, educational attainment, frequency of heroin injection, and use of non-injectable drugs, without great consistency among the studies. Our model is consistent with these previous studies in terms of many of the factors associated with assisting. Our model differs from the multivariable models in the previous studies in that multivariable regression compares the strength of individual factors associated with assisting, and backward elimination will remove many correlated factors from the final model. Our model, in contrast, includes multiple stages so that an individual factor, e.g., non-injecting drug use, may be associated with progression to a later stage, e.g., injection promoting behavior. Our model includes the potential for different factors operating in different temporal stages of the process.

Finally, the formal statement of the model can also be used to assess the strengths and weaknesses of interventions to reduce the likelihood of a current PWID providing assistance with first injections. For these implementations of Break the Cycle in Staten Island and Tallinn, there were significant declines in declining to assist when asked to assist, and a significant decline in injection promotion in Tallinn. These changes are consistent with the motivational interviewing basis of the intervention to focus on and strengthen the participants' existing motivation not to initiate others into injecting drug use.

The model also clarifies some weaknesses in the intervention. Promoting behavior was quite common among the Staten Island participants prior to the intervention and was not significantly reduced, and even though promoting behavior was reduced in Tallinn, it was still common post-intervention among the Tallinn participants. (20% reported engaging in injection promotion during follow-up.)

The lack of any reduction in being asked for assistance indicates two other limitations of this version of Break the Cycle. First, it is likely that the intervention would need to be strengthened and implemented on a very large scale to reduce injection promoting and the demand for assistance within a drug using population. Second, the repeatedly being asked to assist with first injections is likely to wear down resistance to assisting among some intervention participants PWID who would prefer to not provide assistance. Like many behavioral interventions, the effects of Break the Cycle may diminish over time. This could require either providing booster sessions for participants or implementing Break the Cycle on a sufficiently large scale within the PWID culture so that PWID would enforce norms against providing assistance with first injections.

Potential Generalizations and Harm Reduction

We need to be extremely cautious in generalizing from just two sites but want to offer possible generalizations for future research on PWID who do assist with first injections. First, these PWID appear to be greatly involved in both injecting and non-injecting drug subcultures. They not only used non-injected drugs but also have large injecting networks. Second, they reported risky drug use. In both sites, receptive and distributive syringe sharing were associated with engaging in injection promotion. Assisting with a first injection may in itself be considered a health risk behavior. There are the immediate possibilities of a botched injection leading to a skin infection, of an overdose, and of HIV or HCV transmission if sufficient numbers of sterile syringes are not available. And, of course, there are the possibilities of multiple adverse health consequences if the initiate adopts injecting as a regular route of administration.

Given these multiple risks, PWID who assist with first injections would be a particularly appropriate group for engaging in harm reduction activities.

Limitations of the Model

Several limitations of the present model should be noted. First, while the PWID populations in Tallinn and Staten Island are clearly different, these are only two sites. Some modifications of the model may be needed to describe how PWID come to assist with first injections in the very wide variety of PWID populations throughout the world. We suspect there may be possible local site differences in factors associated with engaging in injection promoting and possible additional secondary pathways to assisting.

Second, the model is currently based on cross-sectional data from PWID only. Incorporation of longitudinal dyadic data—from both the non-PWID being assisted with a first injection and from the PWID providing assistance—should extend and strengthen the model.

Next Steps

Initiation into injecting drug use continues as a world-wide public health problem. The current "opioid epidemic" in the US (Scholl et al., 2019) is only the most recent example of rapid expansion of injection drug use. The multi-stage model described here and the clinical trial results of the Break the Cycle—Avant Garde suggest that there is very much that could be done to reduce initiation into injecting drug use. We would suggest the following as next steps:

1. Assessing fit of the model to data from additional PWID populations. If the model is found to apply to initiation into injecting drug use in a wide variety of situations, use the model to guide further research into reducing initiation.
2. Expansion and adaption of Break the Cycle type interventions to many additional areas.
3. Determination if reduced versions of Break the Cycle type intervention might still be effective so that the intervention might be easily implemented on a larger scale.
4. Assess sustainability of effects for Break the Cycle type interventions.
5. Integrate Break the Cycle interventions with interventions to increase NIDUs resistance to injection promoting behaviors. These should include greater access to substance use treatment (including methadone and buprenorphine) so that NIDUs do not initiate injecting because of financial pressures.
6. Socio-behavioral interventions to increase NIDU's motivations to avoid injecting, such as the "Sniffer Project" (Casriel et al.,

1990; ; Des Jarlais et al., 1992) also need to be further researched and then implemented on a public health scale.

7. With the COVID-19 epidemic, many health services for people who use drugs have moved to telehealth platforms. It would be important to determine if behavioral interventions, such as Break the Cycle, that utilized motivational interviewing can also be provided effectively through telehealth.

We believe that the multi-stage model developed here can be utilized to adapt interventions to different drug use settings and to assess the strengths and weaknesses of future interventions to reduce the likelihood that PWID will assist with first injections.

CONCLUSION

We developed a formal multi-stage model of how a current PWID comes to provide assistance with first injections by non-PWID—through engaging in injection promoting behavior, being asked for assistance, and then providing assistance. The model can be subjected to statistical analyses and thus is "falsifiable." The model fit quite well with data from two very different PWID populations, revealed strong similarities in the process of coming to assist with first injections in the two different sites, and can be used to assess strengths and limitations of interventions to reduce the likelihood that current PWID will provide assistance with first injections.

DATA AVAILABILITY STATEMENT

Restrictions apply to the datasets: The datasets presented in this article are not readily available because there are participant identifiers contained within the dataset on a cohort of persons who use drugs. Requests to access the datasets should be directed to the primary author, Don Des Jarlais.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the New York University School of Medicine, Icahn School of Medicine at Mount Sinai, University of Tartu. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

DDJ (Don Des Jarlais) was the Principal Investigator for the study and developed the process model described in the manuscript. He also wrote the original draft of the manuscript and oversaw all data analysis and paper revisions; AU was investigator for the Tallinn Estonia site. DB was the project director for the NYC site, AT and GO oversaw the study site in Estonia, KA, MR, and JF were involved in data analysis, DB, AT, GO, HB, and JF were involved with collection of data for the study, and ST helped to develop the questions for intervention and provided guidance on data collection; all authors reviewed the manuscript draft and approved the final submission.

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Adverse Childhood Experiences Predict Early Initiation of Opioid Use Behaviors

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Introduction: Although a substantial body of research documents a relationship between traumatic stress in childhood and the initiation of substance use later in the life course, only limited research has examined potential linkages between adverse childhood experiences (ACEs) and the initiation of non-medical prescription opioid use and other opioid use behaviors. The present study contributes to this growing body of work by investigating the association of childhood trauma with early initiation of a series of opioid use behaviors.

Methods: New York City young adults ($n = 539$) ages 18–29 who reported non-medical use of prescription opioids or heroin use in the past 30 days were recruited using Respondent-Driven Sampling in 2014–16. Ten ACEs were assessed via self-report with the ACE Questionnaire. Associations between number of ACEs and self-reported ages of initiating seven opioid use behaviors (e.g., non-medical prescription opioid use, heroin use, heroin injection) were estimated with multivariable logistic regression.

Results: Eighty nine percent of participants reported at least one ACE, and 46% reported four or more ACEs, a well-supported threshold indicating elevated risk for negative health consequences. Every increase of one trauma was associated with a 12–23% increase in odds of early initiation across the seven opioid use behaviors. Findings also document that the mean age at initiation increased with increasing risk severity across the behaviors, contributing to evidence of a trajectory from opioid pill misuse to opioid injection.

Discussion: Increasing number of childhood traumas was associated with increased odds of earlier initiation of multiple opioid misuse behaviors. In light of prior research linking earlier initiation of substance use with increased substance use severity, present findings suggest the importance of ACEs as individual-level determinants of increased opioid use severity. Efforts to prevent onset and escalation of opioid use among at-risk youth may benefit from trauma prevention programs and trauma-focused screening and treatment, as well as increased attention to ameliorating upstream socio-structural drivers of childhood trauma.

Keywords: adverse childhood experiences, childhood trauma, opioid misuse, non-medical prescription opioid use, drug use initiation, young adults (18–29 years)

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INTRODUCTION

The epidemic of opioid misuse and associated health consequences, including opioid dependence, overdose, injection drug use, and hepatitis C infection, continues to be a major public health problem in the U.S. Young people are a population of particular concern in this ongoing epidemic. Opioid misuse, like other forms of substance use, is typically initiated in adolescence or young adulthood and often begins with the use of prescription opioids (POs) for non-medical reasons. For members of the Millennial generation in particular, non-medical PO use has played a prominent role in early drug initiation pathways. A recent analysis of 2013–2014 data from the National Survey on Drug Use and Health found that the lifetime prevalence of non-medical PO use was significantly higher - at 21.5% - among Millennials than among members of Generation X or Baby Boomers (Wall et al., 2018). While the prevalence and incidence of PO misuse in adolescents and young adults have declined somewhat in recent years after peaking in 2015 (Substance Abuse and Mental Health Services Administration [SAMHSA], 2020), these rates remain concerning, as do rates of opioid-associated morbidity and mortality in youth. In 2017, overdose fatalities in 15–24 year-olds reached an all-time high of 12.6 deaths per 100,000, with opioids involved in most of these overdoses (Hudgins et al., 2019).

Young people who engage in non-medical PO use are also more likely to use other drugs than youth who have not misused POs. In an analysis of National Survey on Drug Use and Health data from 2015–2016, adolescents and young adults with past-year PO misuse reported high rates of lifetime use of other drugs, including cocaine (35.5%), hallucinogens (49.4%), and inhalants (30.4%) (Hudgins et al., 2019). Research has also established a link between non-medical PO use and subsequent transition to heroin use and injection drug use (Lankenau et al., 2012; Cerda et al., 2015; Kolodny et al., 2015; Carlson et al., 2016; Surratt et al., 2017; Guarino et al., 2018), with up to 80% of new heroin users reporting PO misuse prior to initiating heroin use (Jones, 2013; Muhuri et al., 2013; Hudgins et al., 2019). Evidence indicates that transitions from non-medical PO use to heroin use have become increasingly common over the past two decades; national trend data show a temporal increase from 2002 to 2014 in the odds of heroin use among young people who used PO non-medically (Martins et al., 2017).

Moreover, emerging research suggests that the earlier in the life course PO misuse begins, the greater the risks may be. A national study by McCabe and colleagues found that onset of non-medical prescription drug use before age 14 was a significant predictor of later dependence on prescription drugs (McCabe et al., 2007). Other recent studies have shown that early initiation of non-medical PO use increases the likelihood of transition to heroin use in later adolescence or young adulthood (Cerda et al., 2015; Carlson et al., 2016).

Investigation into the multi-level factors that predispose some youth to initiate non-medical PO use at an early age, and to transition to more severe forms of drug use, has only recently begun. One plausible individual-level risk factor is childhood trauma, as it is well-documented that traumatic stress in childhood can have far-reaching adverse impacts on individuals' psycho-physiological development and well-being. Exposure to traumatic experiences in childhood, ranging from neglect, parental divorce and parental drug use to physical, emotional, and sexual abuse, has shown a strong, graded relationship with risk for a broad range of negative health outcomes in adulthood, from cancer and liver disease to depression, sexual risk behavior and use of illicit drugs (e.g., Felitti et al., 1998; Dube et al., 2006).

Despite a substantial body of research on the relationship between childhood trauma and substance use, only a few studies have examined potential linkages between adverse childhood experiences and the initiation of non-medical PO use or other forms of opioid use over the life course. For example, Merrick et al. (2020) found that experiencing three or more types of adverse experience in childhood significantly increased the risk of PO misuse in adulthood. In one notable study, Quinn et al. (2016) found a dose-response relationship between childhood trauma and PO misuse in which exposure to a greater number of trauma types was associated with progressively increased odds of initiating PO misuse in emerging or later adulthood.

Research exploring the relationship between childhood trauma and age at initiation of opioid or other drug use behaviors is especially limited. Dube et al. (2006) documented a persistent, graded relationship between extent of traumatic exposure in childhood and early initiation of illicit drug use, as well as lifetime risk of engaging in injection drug use, suggesting the additive contribution of multiple types of traumatic experience to the development of drug use problems from adolescence into adulthood (PO misuse was not examined). In another study, childhood sexual abuse among young adult drug injectors was independently associated with earlier age at first injection (Ompad et al., 2005). More recently, Stein et al. (2017)'s study of treatment-seeking persons with opioid use disorder found that exposure to more types of childhood trauma was inversely associated with age at opioid use initiation and positively associated with recent injection drug use and lifetime overdose; reflecting prior research, these were dose-response relationships indicating the cumulative impact of exposure to traumatic stress in early life.

Given the ongoing public health crisis of opioid use, overdose and associated health concerns, it is critically important to better understand the effect of childhood trauma on young people's vulnerability to non-medical PO use and related behaviors. The present study examines the association of number of different types of traumatic childhood experience with age of initiating a range of opioid use behaviors among young adult opioid users in New York City, the vast majority of whom began their opioid use trajectories with the non-medical use of POs. A more complete understanding of these associations may help inform the development and delivery of effective interventions for young people to prevent both the initiation of non-medical PO use and escalation to more severe forms of drug use.

Abbreviations: ACE, adverse childhood experience; DV, dependent variable; HCV, hepatitis C virus; PO, prescription opioid; RDS, Respondent-Driven Sampling.

MATERIALS AND METHODS

Study Population and Procedures

This analysis used data collected from 539 participants recruited from July 2014 through April 2016 for a study of young people's opioid use patterns and trajectories and associated risk behaviors. Participants lived in one of the five boroughs of New York City, were aged 18–29, used POs non-medically and/or heroin in the past 30 days, spoke English, and provided written informed consent. Participants completed a computer-assisted, interviewer-administered interview lasting 90–120 min. Participants received $60 for completing the interview and additional incentives for each eligible participant they referred (see section Recruitment below). The Institutional Review Board of National Development and Research Institutes (NDRI) approved the study. Additional details on study procedures and sample description have been published elsewhere (Mateu-Gelabert et al., 2017; Guarino et al., 2018).

Recruitment

Participants were recruited using Respondent-driven Sampling (RDS), a form of chain-referral sampling designed to engage hard-to-reach populations which uses personal social network connections to drive recruitment (Heckathorn, 1997; Heckathorn et al., 2002). A key feature of RDS is the generation of statistically principled estimates for a sample's target population based on sampling weights that correct for the unequal sampling probabilities inherent in sampling over a social network, as well as standard error estimation correcting for dependence induced by the sampling process (Heckathorn, 1997; Salganik and Heckathorn, 2004).

Using referrals from participants in our previous research ($n = 4$), other research studies ($n = 9$) and service providers ($n = 3$), as well as street recruitment ($n = 4$), a set of 20 eligible opioid users were directly recruited by research staff as RDS "seeds" to initiate recruitment chains. Per standard RDS protocol (WHO/UNAIDS, 2013), seeds were chosen to represent important subgroups of the target population known to researchers. After completing an eligibility screening and the structured interview, each seed was asked to refer to the study up to three eligible peers from their network of fellow opioid users. This peer-referral process was repeated with the seeds' recruits and for successive sampling waves thereafter. Of the 20 seeds, 12 referred eligible peers, thereby initiating recruitment chains. This analysis includes all 20 seeds within the sample of 539.

Independent Variable: Adverse Childhood Experiences

Childhood trauma was assessed with the Adverse Childhood Experiences (ACE) Questionnaire, a 10-item instrument asking whether respondents experienced a broad range of traumatic experiences before the age of 18, including parental divorce, household dysfunction, and physical, emotional, and sexual abuse (see **Table 2** for a list of ACE items and their prevalence in this sample). While a total ACE score of 4 or higher has been found to robustly predict adverse physical and mental health consequences (Felitti et al., 1998; Centers for Disease Control Prevention, 2015), it was included in these analyses as an ordinal variable (range 0–10) to preserve potentially meaningful variation and allow us to investigate the relationship of cumulative trauma to the dependent variables. Additional analyses using a binary ACE independent variable (4 or more vs. 0–3) yielded an extremely similar pattern of results for all seven DVs in unadjusted and adjusted models.

Dependent Variables: Age at Initiation of Opioid Use Behaviors

Seven dependent variables (DV) were explored, all related to age at initiation of opioid drug use and route of drug administration: non-medical use of POs; snorted POs; regular PO use; heroin use; regular heroin use; injected heroin; and injected POs (see **Table 3** for prevalence rates and ages at initiation). Regular use of POs and heroin was defined as one or more times per week for at least 1 month. Age at initiation of each DV was recoded as a binary variable (age in bottom 25th percentile vs. top 75th percentile [referent], that is, younger vs. older age at initiation).

Sociodemographic Covariates

Age, gender, race, ethnicity, and household income during childhood were assessed as potential covariates by estimating their associations with each of the seven DVs in bivariable analyses (results not shown). Only age and gender were significantly associated with DVs (age with seven DVs and gender with three). All multivariable models were adjusted for age (continuous years) and gender (male vs. female [referent]); four transgender respondents' data were coded as missing.

Analytic Strategy

SAS 9.4 (SAS Institute, Cary, North Carolina) was used for univariable descriptive analyses exploring the independent, dependent and socioeconomic variables and for bivariable analyses to identify covariates associated with the DVs. Logistic regression models were run in SAS to get estimated unadjusted (OR) and adjusted (AOR) odds ratios and 95% confidence intervals for the associations between number of ACEs and ages at initiation of the seven opioid use behaviors. Analyses included only those who initiated the behavior before their participation in the study; non-initiates as of the date of interview were excluded from regression models. The strength of each association was assessed by the magnitude of the OR/AOR and the width of the confidence interval.

RDS population estimates were produced in R version 3.2.2 (R Core Team, 2015). As a prerequisite for the calculation of population estimates, multiple imputation was conducted using the R package MICE (Van Buuren and Groothuis-Oudshoom, 2011) to impute missing network size data for a portion of the sample. Target population estimates for key variables were then calculated using the successive sampling estimator (Gile, 2011) in the R package RDS (Handcock et al., 2012), using a working population size of 15,000. Standard statistical tests violate assumptions in the RDS setting because respondents are recruited by other respondents, and pairs or clusters are more or less likely to be similar based on their relative positions in the sampling structure. However, in other analyses using this

TABLE 1 | Socio-demographic characteristics of young adult opioid users in New York City, 2014–16, $N = 539$.

Characteristic	Sample prevalence Percent (%)	Population estimate % (± standard error)
Gender		
Male	67.7	69.7 (4.1)
Female	31.5	29.7 (4.1)
Transgender	0.7	0.5 (0.3)
Ethnicity		
Hispanic/Latino	28.7	29.6 (4.3)
Race		
White	68.8	67.7 (4.5)
Black/African-American	7.8	9.1 (3.3)
Multiracial	8.0	6.1 (1.6)
American Indian or Alaskan Native	1.7	1.5 (0.9)
Asian	1.3	1.5 (0.7)
Did not respond[a]	12.4	14.3 (3.9)
Household income growing up (annual)		
<$50,000	42.1	43.5 (4.7)
$51,000–100,000	32.7	33.0 (4.0)
$101,000 or more	18.9	16.5 (2.7)
Did not respond	6.3	7.1 (2.30)
Age (years) *M (SD)*	24.5 (3.1) NA[b]	

[a] *Missing race data due to Hispanic/Latino respondents reporting ethnicity but not race.*
[b] *RDS package yields only frequency estimates.*

TABLE 2 | Prevalence of adverse childhood experiences (ACE) among young adult opioid users in New York City, 2014–16, $N = 539$.

	Sample prevalence *N* (%)
Type of ACE reported	
Household member depressed/mentally ill	330 (61.2)
Household member went to prison	283 (52.5)
Parents separated/divorced	243 (45.1)
Felt as if no one in the family loved or supported them	229 (42.5)
Lived with someone who had a drinking/drug problem	188 (34.9)
Often felt they did not have enough to eat, were not protected	183 (34.0)
Mother/stepmother physically abused	139 (25.8)
Parent/adult fondled or touched them in a sexual way or had intercourse with them	128 (23.7)
Parent/adult pushed, slapped or threw something at them	106 (19.7)
Parent/adult swore at, humiliated or made them afraid of being physically hurt	89 (16.5)
Total number of ACE types reported (categorical ACE)	
0	58 (10.8)
1–3	234 (43.4)
4–6	159 (29.5)
7–10	88 (16.3)
Total number of ACE types reported (ordinal ACE)	**Mean (SD) Minimum-maximum**
	3.6 (2.6) 0–10

dataset, permutation tests yielded results very similar to standard results (Mateu-Gelabert et al., 2017), alleviating concerns about interdependence impacting estimates. Permutation testing and other methods for analyzing associations in RDS data are in their infancy and do not allow flexibility in how variables are coded or the ability to adjust for covariates in multivariable models. A large body of research findings from studies using an RDS design have used standard analytical tests and presented findings with the caveat that independence assumptions may not hold, as we do here.

RESULTS

Participant Characteristics

Participants were predominantly male (68%), White (69%) and non-Hispanic/Latino (71%), with a mean age of 24.5 years. They represented diverse socioeconomic backgrounds, with 42% reporting an annual household income while growing up of $50,000 or under, 33% reporting $51,000–100,000, and 19% reporting more than $100,000. Full sample demographics, along with RDS-based estimates for the prevalence of these characteristics in the target population of 18–29 year-old opioid users in New York City, are presented in **Table 1**.

Adverse Childhood Experiences

Eighty-nine percent of participants reported at least one adverse childhood experience (**Table 2**). Strikingly, 46% reported four or more adverse experiences (and the mean number of ACEs was 3.6 [SD = 2.6]), putting a large proportion at elevated risk for negative physical and psychological health consequences (Felitti et al., 1998). Prevalence was high among all ACEs, ranging from a low of 17% who reported that a parent or adult swore at or humiliated them or made them afraid of being physically hurt to 61% who had a depressed or mentally ill household member.

Age at Initiation of Opioid Use Behaviors

Nearly all participants had used POs non-medically (only 8 were eligible for the study given their heroin, rather than PO, use), and among those, most initiated non-medical PO use in their teens (83%, not shown in tables), at an average of 16.9 years (**Table 3**). Most progressed to regular PO use (86%) and to snorting POs (73%). The prevalence of PO injection was the lowest (37%) among all DVs. Most participants initiated heroin use (82%) and subsequently reported regular heroin use (79%), and 64% reported heroin injection in their lifetime. The average ages at which participants reported initiating opioid behaviors increased in parallel with the severity of the behavior, from a mean age of 16.9 years at first non-medical PO use to first heroin injection at 20.4 years and first PO injection at 20.6 years.

TABLE 3 | Descriptive statistics for age at initiation of opioid use behaviors among young adult opioid users in New York City, 2014–16.

		Age at first use among initiates (years)		
Opioid use behavior[a]	**Prevalence among total ($n = 539$) N (%)**	**Mean (SD)**	**Minimum-maximum**	**25th quartile**
Non-medical PO use	531 (98.5)	16.9 (3.1)	9–27	15
Snorted PO	394 (73.1)	17.9 (3.1)	10–28	16
Regular PO use	465 (86.3)	18.3 (3.1)	11–28	16
Heroin use	444 (82.3)	19.7 (3.5)	11–29	17
Regular heroin use	423 (78.5)	20.3 (3.4)	9–29	18
Injected heroin	345 (64.0)	20.4 (3.7)	11–29	18
Injected PO	197 (36.6)	20.6 (3.6)	13–28	18

[a] *PO, prescription opioid.*

TABLE 4 | Associations of number of adverse childhood events (ACE)[a] and age at initiation of opioid use behaviors among young adult opioid users in New York City, 2014–16.

Opioid use behavior[b]	**Odds ratios for younger age at drug initiation** ***Referent = age in top 75th percentile***	
	OR (95% CI)[c]	**AOR (95% CI)**[d]
Non-medical PO use	1.22 (1.12, 1.32)	1.23 (1.12, 1.43)
Snorted PO	1.15 (1.05, 1.26)	1.16 (1.05, 1.28)
Regular PO use	1.20 (1.09, 1.32)	1.22 (1.10, 1.36)
Heroin use	1.20 (1.07, 1.43)	1.17 (1.03, 1.32)
Regular heroin use	1.15 (1.05, 1.26)	1.14 (1.03, 1.25)
Injected heroin	1.15 (1.05, 1.27)	1.13 (1.02, 1.25)
Injected PO	1.18 (1.03, 1.35)	1.12 (0.97, 1.30)

[a] *ACE modeled as ordinal variable with range 0–10.*

[b] *PO, prescription opioid.*

[c] *OR, odds ratio; CI, confidence interval; estimates represent the increase in odds of initiating drug use at younger age (bottom 25th percentile) for every 1-unit increase in ACE number.*

[d] *AOR, adjusted odds ratio; multivariable models include gender and age.*

Relationships Between Number of ACEs and Age at Initiation of Opioid Use Behaviors

In unadjusted models, ACE number was significantly associated with younger age at initiation of opioid use behavior for all seven DVs. The increase in odds associated with every increase of one trauma ranged from 15 to 22% (**Table 4**). This pattern and the strength of the associations was very similar in multivariable models adjusted for age and gender. ACE number was significantly associated with six DVs, and the increased odds ranged from 13 to 23%. Only the association for PO injection was not statistically significant; the inclusion of the covariates as well as the small sample size due to the relatively low prevalence of this behavior ($n = 196$, 37%) likely affected the ability to observe a non-null association.

DISCUSSION

In this large, RDS-based study of opioid-using young adults, adverse childhood experiences were highly prevalent, and number of traumatic exposure types was significantly associated with early onset of a broad range of opioid use behaviors, providing further support for an additive effect of exposure to different types of trauma on the initiation and development of youth's substance use trajectories. Earlier substance use initiation has been linked in multiple studies to the development of greater-severity drug use problems and progression to riskier forms of use, such as heroin use and drug injection (McCabe et al., 2007; Grella and Lovinger, 2011; Cerda et al., 2015; Carlson et al., 2016). This knowledge, coupled with our findings and other emerging evidence of trauma's association with opioid misuse, highlights the need to incorporate prevention and early detection of trauma into drug use prevention and treatment programs.

The prevalence of adverse childhood experiences among young adults in this study, with 89% of participants reporting at least one traumatic experience and nearly half reporting 4 or more types of trauma, is markedly higher than for general population samples (64% with 1 ACE and 12% with 4 or more; Centers for Disease Control Prevention, Kaiser Permanente, 2016) and many other substance-using populations, but roughly comparable to rates reported for other opioid-dependent groups. A study of the trauma profiles of non-treatment-seeking, substance-dependent adults found a much higher prevalence of childhood trauma in the PO-dependent group (90%) than in the cocaine-dependent group (60%; Lawson et al., 2013). In another study, 80% of opioid-dependent outpatients seeking buprenorphine treatment reported any experience of childhood trauma (Sansone et al., 2009). Similarly, this sample's mean ACE score (3.6, SD = 2.6) is remarkably close to that reported in a recent study of treatment-seeking persons with opioid use disorder (3.64, SD = 2.75; Stein et al., 2017). Taken together, these findings suggest that opioids may be particularly appealing as a drug of choice for individuals with a history of trauma as they may exert a similar palliative effect on psychological pain as they do on physical pain (Rosenblum et al., 2008). There is some compelling qualitative evidence to support this; Scottish drug injectors reported that "heroin injection was an effective means of blotting out distressing thoughts and feelings" related to early trauma (Hammersley et al., 2016).

Of particular note are the findings demonstrating a consistent, gradient pattern of association in which each one-unit increase in ACE score is associated with increased odds (ranging from

12 to 23%) of early initiation across opioid use behaviors. These findings support and extend the results of previous research that has found childhood trauma to have strong, dose-dependent relationships with early initiation of illicit drug use, including opioid misuse, and the likelihood of engaging in injection drug use and experiencing non-fatal overdose (Dube et al., 2006; Felitti and Anda, 2009; Stein et al., 2017), as well as with younger age at first injection (Ompad et al., 2005).

The present study contributes to emerging research on childhood trauma and opioid misuse by focusing on the new generation of young opioid users who were introduced to opioids via the non-medical use of POs. The predominance of males and Whites in the sample is consistent with the demographic patterns of PO misuse among U.S. young adults in 2014–2016, when these data were collected (Hudgins et al., 2019). However, more recent national data suggest that these demographic patterns may be shifting. For example, in 2019, more female than male, and more Black and Hispanic than White, high school students reported both current and lifetime PO misuse (Jones et al., 2020).

The study also advances existing research by documenting associations of childhood trauma with earlier initiation of a series of interrelated forms of opioid use, from first experience of non-medical PO use, first intranasal PO use, and initiation of regular PO misuse to first heroin use, onset of regular heroin use, first heroin injection, and first PO injection. Knowledge of the substantial co-occurrence among these opioid use behaviors, indeed a trajectory of behaviors that put individuals at progressively greater risk of not only opioid use disorder and overdose, but also HCV, HIV and bacterial infections (for those who progress to injection), is valuable information that may help optimize the content and timing of prevention, treatment and harm reduction programming for young populations. Other analyses of this dataset have shown that PO injection is associated with elevated risk for overdose and HCV infection relative to heroin injection (Mateu-Gelabert et al., 2020), further supporting the concept of a trajectory of opioid use behaviors characterized by escalating severity and increasing health risks.

A potential mechanism underlying the observed associations between adverse childhood experiences and early non-medical PO use and other opioid use behaviors, is self-medication, in which individuals use psychoactive substances as a form of avoidant coping, to alleviate distressing emotional states resulting from traumatic experience (Khantzian, 1997; Khantzian and Albanese, 2008). Given the established associations between early drug use initiation and greater problem severity, earlier onset of PO misuse may in turn increase the likelihood of earlier progression to greater-intensity use and earlier transition to heroin use and drug injection, effectively priming youth for an accelerated trajectory of opioid and, frequently, poly-substance use. Additionally, a wide-ranging body of research has shown that exposure to traumatic stress early in life can interfere with typical developmental processes, potentially leading to neurocognitive, psychological and social impairments (Weiss and Wagner, 1998; U.S. Department of Health Human Services, 2001). Thus, the negative impacts of early opioid misuse on youth development may compound the deleterious effects of early traumatic exposure. Clarifying the behavioral and psychosocial pathways from adversity to drug use initiation is a crucial next step for research in this area, as is investigation into their interactive effects. Future research should also examine the impact of specific types of adverse childhood experiences on the likelihood of early onset and age at initiation of opioid misuse behaviors.

Limitations

Given the cross-sectional nature of this study, findings only establish correlation, not causation. Therefore, caution is warranted in attributing differences in age of initiation to childhood trauma; however, the consistency of present results with prior research does support this interpretation. Generalizability of findings is limited by the inclusion in the sample of residents of New York City only, who likely differ socio-demographically and perhaps in terms of trauma exposure and drug use patterns from other U.S. subpopulations. Nonetheless, understanding this urban population's risk factors and drug use trajectory is critical given the city's size and ongoing opioid epidemic. Bias may also have been introduced by the use of RDS as a recruitment methodology, due to the dependence in the sample (as participants are recruited by other participants), as well as by the non-random selection of participants to serve as RDS seeds. Another limitation concerns the nature of self-report data, which may be vulnerable to recall and social desirability bias. We were not able to investigate the contribution of age of traumatic experience to early initiation because of challenges in linking traumatic experiences to specific dates. Indeed, recall bias that stems from asking adults about childhood experiences and difficulties in asking young children about adversity pose challenges for clarifying the influence of age of trauma on subsequent outcomes, but this is an important next step that is needed to clarify pathways and inform prevention and treatment strategies. Finally, although the goal of this analysis was to investigate the combined role of a broad range of traumatic events, the relationship of particular events to opioid initiation are also worthy of exploration.

Public Health Implications

These findings underscore the importance of prevention, early detection and treatment of both childhood trauma and opioid misuse among youth. Pediatricians, adolescent medicine specialists and others who work with youth should be made aware of the close links between traumatic exposure and early-onset use of POs and other drugs (both pharmaceutical and illicit), so they can incorporate screening for both into their practice as appropriate. Focused efforts to address trauma-related issues early in the life course may serve as a means to prevent or delay the uptake of opioid and other substance use. Interventions for groups vulnerable to adversity could promote resilience as a way of buffering youth from the far-reaching negative impacts of traumatic stress. The high prevalence of adverse childhood experiences documented among opioid-using young adults in this and other research suggests that routine screening for early traumatic exposure among young people seeking treatment for opioid use disorder may be warranted, so that integrated – and potentially more effective – mental health and substance use treatment can be delivered. Results further suggest the potential value of developing and implementing trauma-informed behavioral interventions for opioid-using adolescents and young adults. Training youth in adaptive coping skills to better manage the psychosocial and emotional repercussions of traumatic stress may enhance efforts to prevent escalation of use, transition to heroin and/or injection drug use and exposure to HIV and HCV. However, such individual-level interventions should not substitute for the larger project of ameliorating the upstream socio-structural conditions that help perpetuate childhood trauma and distribute its harms inequitably, often exacting the greatest toll on those most vulnerable.

DATA AVAILABILITY STATEMENT

The dataset presented in this article is not readily available due to the sensitive nature of the dataset (containing information about illegal drug use, sexual behavior, HIV and HCV status, etc.) and the potentially damaging consequences to study participants if their identities were to become known; therefore, the data cannot be shared outside the research team. Requests to access the dataset should be directed to Honoria Guarino, honoria.guarino@sph.cuny.edu.

ETHICS STATEMENT

The study involving human participants was reviewed and approved by National Development and Research Institutes Institutional Review Board. The participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

PM-G and SS conceptualized the general approach of this study and KR conducted initial analyses. KQ and HG revised the analytic plan and KQ conducted the final analyses reported here. CS, EG, and LJ collected the data on which the study is based. SS made significant contributions to initial literature reviews and an early version of the manuscript. HG wrote the current version of the manuscript, with assistance from KQ, particularly in the Methods and Materials and Results sections. SF provided critical feedback on an interim version of the manuscript. All authors have contributed to revising and have approved the manuscript.

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Chronic High Risk Prescription Opioid Use Among Persons With HIV

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Persons with HIV (PWH) are a population at risk for adverse sequelae of opioid use. Yet, few studies have examined correlates of chronic high risk opioid use and its impact on HIV outcomes. Trends in prescribing patterns and identification of factors that impact the use of opioid prescriptions among PWH are crucial to determine prevention and treatment interventions. This study examined electronic medical records (EMR) of patients receiving HIV care to characterize prescribing patterns and identify risk factors for chronic high risk prescription opioid use and the impact on HIV outcomes among PWH in primary care from July 1, 2016–December 31, 2017. EMR were analyzed from 8,882 patients who were predominantly male and ethnically and racially diverse with half being 50 years of age or older. The majority of the 8,744 prescriptions (98% oral and 2% transdermal preparations) given to 1,040 (12%) patients were oxycodone (71%), 8% were morphine, 7% tramadol, 4% hydrocodone, 4% codeine, 2% fentanyl, and 4% were other opioids. The number of monthly prescriptions decreased about 14% during the study period. Bivariate analyses indicated that most demographic and clinical variables were associated with receipt of any opioid prescription. After controlling for patient socio-demographic characteristics and clinical factors, the odds of receipt of any prescription were higher among patients with pain diagnoses and opioid use and mental health disorders. In addition, the odds of receipt of high average daily morphine equivalent dose (MED) prescriptions were higher for patients with pain diagnoses. Lastly, patients with substance use disorders (SUD) had an increased likelihood of detectable viral load compared to patients with no SUD, after adjusting for known covariates. Our findings show that despite opioid prescribing guidelines and monitoring systems, additional efforts are needed to prevent chronic high risk prescriptions in patients with comorbid conditions, including pain-related, mental health and substance use disorders. Evidence about the risk for chronic high risk use based on prescribing patterns could better inform pain management and opioid prescribing practices for patients receiving HIV care.

Keywords: opioid prescription, morphine equivalent daily dose, chronic opioid therapy, HIV, viral suppression

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INTRODUCTION

Despite large-scale investments at the national, state and local levels to address the opioid epidemic in the U.S., including efforts to promote judicious opioid prescribing, persons with HIV (PWH) remain at risk for adverse sequelae of prescription opioid use, including chronic opioid use, dependence, and overdosage. Studies over the last decade consistently show that PWH have a high prevalence of chronic pain at all stages of HIV and have a high prevalence of undertreatment of pain (Parker et al., 2014; Kowalski et al., 2015). Chronic pain in PWH includes the classically described syndromes of HIV associated neurologic diseases (HAND) and avascular necrosis, and also a high burden of regional and diffuse musculoskeletal pain (Robinson-Papp & Simpson, 2009; Mazzotta et al., 2011; Miaskowski et al., 2011; Merlin et al., 2016). While guidelines emphasize the primary role of non-pharmacologic and non-opioid pharmacologic interventions to promote safe and effective chronic pain management, PWH are more likely to have received opioid prescriptions, at higher doses, and for longer periods compared to the general population (Edelman et al., 2013; Canan et al., 2018; Merlin et al., 2018; Canan et al., 2019; Lemons et al., 2019). Among patients receiving HIV care, between 17 to 53% received opioid prescriptions, (Silverberg et al., 2012; Edelman et al., 2013; Koeppe et al., 2013; Jeevanjee et al., 2014; Merlin et al., 2016; Canan et al., 2018; Flores et al., 2018; Canan et al., 2019; Edelman et al., 2020), and estimates indicate that between 2-65% report misusing them (Newville et al., 2015; Lemons et al., 2019) and between 8-17% have chronic opioid prescriptions (Merlin et al., 2016). Medicaid claims data from 2001-2009 showed that the odds of chronic opioid use was 3 times higher among PWH compared to those without HIV(Canan et al., 2019). Additionally, estimates of the prevalence of opioid use disorders (OUD) among PWH show higher rates compared to people without HIV (Edelman et al., 2013; Hartzler et al., 2017). Jurisdictions and health care providers face challenges in ensuring effective chronic pain management while preventing and addressing opioid misuse, OUD and opioid related morbidity and among PWH.

PWH often present with concomitant health conditions that cause chronic pain and consequently require pain management. Evidence demonstrates that an estimated 25–80% of PWH report health conditions and disorders associated with chronic pain (Tsao et al., 2010; Dowell et al., 2016; Dowell et al., 2016; Bruce et al., 2017). These conditions may require prescription opioid use to improve overall function and well-being, if first line non-pharmacologic and non-opioid pharmacologic treatments have been unsuccessful in relieving pain and restoring function (Robinson-Papp et al., 2010; Miaskowski et al., 2011; Parker et al., 2014; Kowalski et al., 2015; Merlin et al., 2016; Merlin et al., 2018).

Concurrently, PWH have a high prevalence of multilevel risks and exposures, which may increase the likelihood that prescribed opioids may be misused or may otherwise complicate or compromise HIV treatment outcomes, such as engagement in care, adherence to antiretroviral therapy (ART), and maintenance of viral load (VL) suppression (Robinson-Papp et al., 2012). The prevalence of mental health and substance use disorders among PWH exceed those in the general population (Petry, 1999; Turner et al., 2001; Chander et al., 2006; Samet et al., 2007; Sohler et al., 2007; Tsao et al., 2007; Pence et al., 2008; Altice et al., 2010; Azar et al., 2010; Hahn & Samet, 2010; Justice et al., 2010; Tsao et al., 2011; Tsao et al., 2012; Merlin et al., 2016). Approximately half of PWH have a history of mental health or substance use disorders. Data show that 5–33% drink alcohol at hazardous levels, (Beltrami et al., 2000; Cook et al., 2001; Galvan et al., 2002; Conigliaro et al., 2003; Chander et al., 2006; Braithwaite et al., 2007; Chander et al., 2008; Bertholet et al., 2010; Green et al., 2010; Justice et al., 2010; Marshall et al., 2015; Crane et al., 2017; Bensley et al., 2018), between 22-40% report use of illicit drugs, (Bing et al., 2001; Tucker et al., 2003; Chander et al., 2008; Korthuis et al., 2012), and 8–48% meet criteria for substance disorders(Dew et al., 1997; Cook et al., 2001; Samet et al., 2007; Tsao et al., 2007; Green et al., 2010; Proeschold-Bell et al., 2010; Robinson-Papp et al., 2012; Tsao et al., 2012; Marshall et al., 2015; Newville et al., 2015; Hartzler et al., 2017; Williams et al., 2017; Williams et al., 2018). In a study of opioid prescriptions using a random sample of records of commercially insured patients in the U.S., Shah and colleagues found that transitions from initiation of prescription opioid pain management to chronic opioid use occur very quickly (Shah et al., 2017). Examination of the first month of prescriptions showed that the risk for chronic use increases within three days of initiating prescription opioid use, and the likelihood of use beyond a year doubles just after seven days of use.

However, gaps in knowledge persist about correlates of chronic high risk opioid prescriptions among PWH, (Merlin et al., 2016; Canan et al., 2018), and data of its impact on HIV outcomes are limited (Cunningham, 2018; Flores et al., 2018). Additionally, the limited studies on the impact of prescription opioid use on adverse HIV outcomes have shown conflicting results (Cunningham, 2018). Studies have found either no effect on VL suppression with prescribed opioids (Önen et al., 2012; Koeppe et al., 2013; Newville et al., 2015; Merlin et al., 2016; Canan et al., 2018; Schranz et al., 2019) or a protective effect on virologic failure (VL > 1000 copies/mL) with long-term (at least 90 consecutive days) chronic prescriptions (Merlin et al., 2018). However, in a large retrospective study that examined the association between opioid prescriptions and VL using medical records at a large healthcare system, virologic failure was more likely among patients with an opioid prescription, even after accounting for known predictors of high VL (Flores et al., 2018). Additionally, adverse outcomes (e.g., non-adherence to ART, higher VL) were found when comparisons involved repeat prescriptions or misuse of opioids(Robinson-Papp et al., 2012; Önen et al., 2012; Jeevanjee et al., 2014; Lemons et al., 2019). Mechanisms of how use of opioid analgesics impacts HIV outcomes are poorly understood (Cunningham, 2018) with assumptions about patient motivation to maintain a prescription as a potential driver for engagement and retention in HIV care and ART adherence, on one hand, and problematic opioid use as the premise for poor engagement in care and adherence, on the other hand, which is consistent with empirical evidence on substance use disorders (SUD) and adverse HIV outcomes more generally. Examination of trends in prescribing patterns and identification of factors that impact the course of prescribed opioid use among PWH are crucial, particularly given their potential to identify both trajectories that move from short term low risk use to chronic high risk use and how these, in turn, may impact HIV outcomes (Flores et al., 2018).

This study sought to characterize opioid prescription patterns and identify risk factors for chronic high risk opioid prescriptions and HIV outcomes among PWH in primary care. The study involved electronic medical records (EMR) from a large health system with a comprehensive HIV treatment center in NYC during a period following the dissemination of a set of opioid prescribing guidelines designed to curtail the epidemic. In March 2016, the CDC updated the 2014 national recommendations on opioid prescriptions for primary care clinicians treating adult patients with non-cancer chronic pain specifying the importance of risk assessments, prescription initiation or continuation, appropriate drug and dosing, and ongoing assessments for and linkage to OUD and SUD treatment (Dowell et al., 2016; Dowell et al., 2016). Additionally, laws in NY State were updated in 2016 to limit prescriptions to seven days for acute pain, adding to the 2013 mandate for the state's prescription monitoring program (I-Stop) for physicians to review a patient's opioid prescription history and set of recommendations for patients discharged from emergency departments (Public Health Article 33, 2016). Thus, this study was uniquely positioned to examine trends in opioid prescribing practices to assess short-term impact of public health policies to curb the opioid epidemic.

METHODS

Data Source

EMR data from patients receiving HIV care at the Mount Sinai Institute for Advanced Medicine (IAM) in New York City were extracted for retrospective analysis. The IAM is comprised of five ambulatory care centers which provide comprehensive care to persons with HIV who are predominately uninsured or receive federal or state assistance (e.g. Medicaid, Medicare, and Ryan White). The IAM provides primary care and specialty care in cardiology, dermatology, nephrology, neurology and psychiatry, as well as support services for mental health and social services, case management, and coordinated clinical care. EMR documented clinical encounters occurring between July 1, 2016–December 31, 2017 for patients who met the following study inclusion criteria we included for analysis: 1) age ≥18 years, 2) confirmed HIV diagnosis, and 3) at least one primary care visit during the study period.

EMR were collected using Microsoft Access to query Epic Clarity, a reporting database that interfaces with the Epic EMR system. Data tables containing patient- and encounter-level records were managed in Access. De-identified datasets were imported into SPSS (version 24) for data cleaning and analysis. Manual chart reviews of subsets of cases were conducted to verify records as needed. The Institutional Review Board at Mount Sinai approved procedures for this study.

Variables Extracted

Patient socio-demographic data extracted included age, gender, ethnicity and race. Age was not normally distributed and was skewed with 74% of patients being 40 years of age or older and thus, we categorized the variable into 4 age groups (18–29, 30–39, 40–49, and 50+) and also dichotomized (<40 and ≥40). Gender was collapsed into 3 groups from the 4 gender identity groups attained from the EMR: 1) cisgender and transgender male (n = 6,846); 2) cisgender female (n = 1,970); and 3) transgender female (n = 66). Due the small number of transgender males (n = 3), records were combined with those of cisgender males (n = 6,843) for a total of 6,846. Ethnicity and race were combined into one variable and collapsed as non-Hispanic African-American or Black, Hispanic, non-Hispanic White, Asian or Pacific Islander, and mixed or other.

The variable "years since HIV diagnosis" was not normally distributed and had a platykurtic distribution with negative kurtosis values. Thus, the variable was categorized into 3 groups based on the number of years with an HIV diagnosis (<5 years, between 5 and <10 years, and ≥10 years). Chart reviews were conducted to verify diagnosis date for most patients; however, diagnosis dates could not be determined for 2,430 patients. Diagnosis codes based on International Classification of Diseases-9/10-Clinical Modification (ICD-9/10-CM) codes were utilized to identify deceased patients and patients with non-opioid SUD, OUD, mental health disorders (adjustment, anxiety, bipolar, depression, eating, gender identity, neurocognitive, neurodevelopmental, obsessive compulsive, personality, psychotic, sexual, sleep, trauma), and pain disorders. Data on recent substance use (in the 6 months prior to clinic visit) were extracted from substance use screening, completed at the time of an encounter. Providers or clinical team members asked patients at the time of a primary care visit about the use of different illicit substances and misuse of prescriptions and alcohol. Viral load and CD4 count were recorded using the first laboratory result available during the study period, and the variables were categorized into virally suppressed (<50 copies/mL) vs. unsuppressed (≥50 copies/mL) and CD4 counts were dichotomized as <200 or ≥200.

A total of 18,296 records of opioid analgesic prescriptions, excluding any methadone and buprenorphine formulations, prescribed to eligible patients were extracted from EMR. Given that we could not determine from the extracted EMR whether methadone and buprenorphine were prescribed to treat pain vs. to treat opioid use disorders, as they are commonly prescribed, we excluded records of patients receiving methadone or buprenorphine for the purposes of this study. Prescription records included brand and generic name, date ordered, start and end date of prescription course, dosage, and quantity to be dispensed (e.g., number of tablets). Some prescriptions documented in the EMR had a 'discontinuation indicator, with categories including discontinued by another clinician or patient; patient refusal, non-compliance or transfer; changed due to drug interactions or side effects; formulary or dose change; and indication that therapy was completed; or prescription entry errors. We then validated opioid prescriptions through a multi-step chart review process. For a record to be determined to be valid, either of the following criteria had to be met: an electronically confirmed receipt by the pharmacy, or a prescription for opioids was refilled during the study period. A subsample of 50 records was randomly selected for each discontinuation category and chart reviewed to determine whether each of those prescriptions was valid. If all of the records in the subsample for a particular discontinuation category were found to be valid, then all of the prescriptions for that category were considered valid and included in analysis (this was the case for the categories discontinued by another clinician, alternate therapy, side effects, duplicate medication, and entry error). If not all records in the subset of any given discontinuation category were considered valid, then the full dataset of records for those specific categories were chart reviewed to determine validity for each prescription record (this was the case for the categories patient discontinued, dose adjustment, and "other"). A total of 7,548 (41.3%) of all opioid prescriptions were deemed invalid (for the reasons delineated above) and were excluded. Additionally, 2,004 prescription records were excluded for patients with a cancer diagnosis. Thus, a total of 8,744 prescriptions were included for data analysis.

To account for differences in opioid drug type and dose, we calculated each patient's average daily morphine equivalent dose (MED) based on CDC's standardized measure that considers morphine conversion factor for the opioid drug type, dose, number dispensed, and days supplied (Dowell et al., 2016; HHS Office of Inspector General, 2020). Of the 8,744 opioid prescriptions included in analysis, 1,508 (17.3%) prescription records had to be excluded in calculating the MED variable because start and end dates for those prescriptions had incomplete or erroneous information. Additionally, MED was not computed for 186 (2.1%) transdermal prescriptions. For 7,050 records with valid prescription dates, we aggregated the total number of days supplied for each patient. Long term opioid prescriptions were defined as those extending >365 days.

Outcomes

The three outcomes were receipt of any opioid prescription, receipt of chronic high MED, and unsuppressed VL. We defined receipt of any opioid prescription as a record of an opioid analgesic prescription regardless of days supplied or dosage. Chronic high MED prescription receipt was defined as having received a prescription with daily dosage of >120 MED for ≥30 consecutive days (Dowell et al., 2016; Canan et al., 2018; Merlin et al., 2018; HHS Office of Inspector General, 2020). Unsuppressed VL was defined as having a viral load ≥50 copies/mL (Thompson et al., 2020).

Data Analysis

Descriptive statistics were calculated with percentages for categorical variables and means and standard deviations (SDs) for continuous variables. Opioid prescriptions were aggregated by month and trends in prescribing (number of prescriptions per month, median MED per month, and percentage of prescriptions per month) were summarized by subgroup, in terms of age group, gender, race/ethnicity, and pain diagnosis, differentiating all subgroups by low (≤120) and high (>120) MED. Chi-square tests for bivariate analyses examined differences in characteristics of patients who had or had not received ≥1 opioid prescription. Bivariate associations between each outcome and patient-level factors were examined in separate unadjusted logistic regressions. To identify patient-level factors associated with each outcome, separate stepwise multivariate linear regression models were conducted incorporating age, gender, race/ethnicity, years since HIV diagnosis as a categorical variable, pain diagnosis, SUD, OUD, and mental health disorders. The model predicting high VL also included the effect of MED to compare high MED prescriptions to no prescriptions and low MED. Statistical analyses were performed in SPSS version 24.

RESULTS

Socio-Demographic and Clinical Characteristics

Table 1 presents the demographic and clinical characteristics of the 8,882 patients who had at least one HIV primary care visit from July 1, 2016 - December 31, 2017. Patients were predominantly male and ethnically and racially diverse. Half of the sample was 50 years of age or older with 39% having been diagnosed with HIV for 10 or more years. About 80% were virally suppressed (<50 copies/mL) and 91% had a CD4 count ≥200 based on the first available laboratory result during the study period. Additionally, 28% had documentation of a pain diagnosis, and nearly 39% had a mental health disorder, including depressive (21%), anxiety (13%), sleep (6%), bipolar (4%), and adjustment disorders (3%). EMR documentation of recent substance use during primary care visits was made for approximately 30% of patients (2694/8882); 16% (454/2694) of those screened reported alcohol or drug use in the 6 months prior to a visit, representing 5% (454/8882) of all patients.

Overall, 1631 (18%) patients had documentation of ≥1 SUD; of those, 23% had OUD, 31% alcohol, 31% cocaine, 23% cannabis, 18% amphetamine use disorders, and 19% other or unspecified substances (results not shown in tables). A greater percentage of men had documentation of an alcohol or an amphetamine use disorder compared to cisgender and transgender women (6 vs. 4% and 3% for alcohol; 4 vs. 0.3% and 1% for amphetamine, respectively; all $p < 0.01$), while a greater percentage of cisgender and transgender women had documentation of an OUD excluding heroin compared to men (5 and 5% vs. 3% for opioid, respectively; all $p < 0.05$, results not shown in tables).

Opioid Prescription Trends

During the 18-month study period, 8,744 opioid prescriptions (98% oral and 2% transdermal opioid preparations) were provided to 1,040 (12%) patients (results not shown in tables). The majority (71%) of prescriptions were oxycodone, 8% were morphine, 7% tramadol, 4%

TABLE 1 | Socio-Demographic and Clinical Characteristics of People in HIV Care who Received ≥1 Opioid Prescription, July 2016-December 2017 (*n* = 8,882).

	Any opioid prescription						
	Total		**Yes**		**No**		
	(*n* = 8,882)		**(*n* = 1,040, 11.7%)**		**(*n* = 7,842, 88.3%)**		
	N	**(%)**	**n**	**(%)**	**n**	**(%)**	***p***
Age, years (M, SD, min-max)	(48.02,12.68,18–92)		(53.61,10.70,19–85)		(47.27,12.74,18–92)		
18–29	848	9.5	36	4.2	812	95.8	***
30–39	1674	18.8	81	4.8	1593	95.2	
40–49	1897	21.4	186	9.8	1711	90.2	
50+	4463	50.2	737	16.5	3726	83.5	
Gender							
Male	6846	77.1	654	9.6	6192	90.4	***
Cisgender female	1970	22.2	368	18.7	1602	81.3	
Transgender female	66	0.7	18	27.3	48	72.7	
Ethnicity/Race							
Non-hispanic african-american	2988	33.6	377	12.6	2611	87.4	***
Hispanic	2163	24.4	326	15.1	1837	84.9	
Asian or pacific Islander	151	1.7	5	3.3	146	96.7	
Other/Multiple	1680	18.9	157	9.3	1523	90.7	
Non-hispanic white	1900	21.4	175	9.2	1725	90.8	
Years since HIV diagnosis (M, SD, min-max)	(12.57,9.15,0–41.50)		(16.40,9.08.02–36.5)		(12.06,9.04,0–41.5)		
<5 years	1836	20.7	108	5.9	1728	94.1	***
5 < 10 years	1388	15.6	148	10.7	1240	89.3	
≥10 years	3449	38.8	523	15.2	2926	84.8	
Missing	2209	24.9					
Death during study period							
Yes	46	0.5	15	32.6	31	67.4	***
No	8636	99.5	1025	11.6	7811	88.4	
HIV viral suppression							
Suppressed (<50 copies/mL)	7048	79.4	815	11.6	6233	88.4	ns
Unsuppressed (≥50 copies/mL)	1698	19.1	218	12.8	1480	87.2	
Missing	136	1.5					
CD4							
<200 cells/mL	625	7.0	106	17.0	519	83.0	***
≥200 cells/mL	8081	91.0	925	11.4	7156	88.6	
Missing	176	2.0					
Pain diagnosis							
Yes	2522	28.4	610	24.2	1912	75.8	***
No	6198	69.8	418	6.7	5780	93.3	
Substance use disorder (excluding opioid use disorder)							
Yes	1428	16.1	213	14.9	1215	85.1	***
No	7454	83.9	827	11.1	6627	88.9	
Opioid use disorder							
Yes	367	4.1	99	27.0	268	73.0	***
No	8515	95.9	941	11.1	7574	88.9	
Substance use in past 6 months							
Yes	454	5.1	63	13.9	391	86.1	ns
No	2240	25.2	306	13.7	1934	86.3	
Missing	6188	69.7					
Mental health disorder							
Yes	3426	38.6	526	15.4	2900	84.6	***
No	5456	61.4	514	9.4	4942	90.6	

*[a]Includes 6,843 cisgender and 3 transgender males; *p < .05; **p < .01; ***p < .001.*

M = mean; SD = standard deviation; min-max = minimum and maximum values; ns = nonsignificant.

hydrocodone, 4% codeine, 2% fentanyl, and 4% were other opioids. The median daily dosage was 46.55 MED (M = 75.55, SD = 89.80); 5,606 (80%) prescriptions were low MDE and 1,444 (20%) were high MDE. **Figure 1** depicts trends in monthly prescriptions by age group, gender, race/ethnicity, and pain diagnosis by low and high MED subgroups. Over the study period, the number of monthly prescriptions decreased by 14.1%, from 526 prescriptions in the first month (July, 2016) to 452 prescriptions in last month (December, 2017). However, while low MED (≤120) decreased by 14.2% from 345 to 296 prescriptions, high MED increased by 18.3% from 71 to 84 prescriptions. Median MED decreased by 7% overall from 48.21 to 44.72; however, the decrease occurred in the low MED subgroup; the median MED among the high MED subgroup remained stable during the study period. Percentages of monthly prescriptions by age, gender and race/ethnicity, and pain diagnosis showed similar trends among subgroups with the exception of inflections in prescriptions among younger (<40 years) patients and transgender women.

Univariate Analyses

Among all patients, 1040 (12%) patients had at least one opioid prescription; 8% of patients received prescriptions for oxycodone, 2% for tramadol, and 2% for other opioids including codeine, fentanyl, hydrocodone, hydromorphone, morphine, oxymorphone, tapentadol, and tramadol (results not shown in tables). Among those with a prescription, 36% of patients received just one opioid prescription, 20% had 2-3 prescriptions and 44% had ≥4 prescriptions during the 18-month study period. Bivariate analyses indicated that most demographic and clinical variables, with the exception of VL suppression, were associated with receipt of any opioid prescriptions (**Table 1**). Older age and identifying as *cis*-gender female, transgender female, Black/African American or Hispanic were associated with receipt of any prescriptions. Similarly, having been diagnosed with HIV for 10 or more years, a CD4 count <200, and documentation of having died during the study period were associated with having received ≥1 prescription. Furthermore, having documentation of a mental health disorder, an OUD, and a SUD including alcohol or drugs other than opioids were each associated with having received ≥1 prescription. Among the 2694 patients who were asked about recent substance use during their primary care visit, a similar percentage of patients (~14%) with or without recent substance use received prescriptions. No significant associations were found between having received prescriptions and use of specific substances, except that a lower percentage of patients who reported using crystal methamphetamine received prescriptions compared to patients with no crystal methamphetamine use (5 vs. 14%, $p = 0.03$).

Analyses of daily dosage of >120 MED and long-term opioid prescription receipt (>1 year) showed several statistically significant trends among the patients with available prescription data. Long-term opioid prescriptions were found among 311 (40%) of 776 patients. Nearly 43% of patients 40 years of age or older had prescriptions for a year or longer compared to 5% of younger patients ($p < 0.001$). A larger percentage of patients with long-term prescriptions had diagnosed HIV longer than 5 years (47% 10 or more years, 28% between 5 and 10 years and 16% less than 5 years; $p < 0.001$) and had a pain diagnosis (49 vs. 26% no pain diagnosis, $p < 0.001$). Additionally, of the 772 patients with available MED data, 109 (14%) patients received a high daily dose and 663 (86%) patients had prescriptions with a daily dosage ≤120 MED Receipt of chronic high MED opioid prescriptions was associated with older age and pain diagnosis. More patients ≥40 years of age received a high-dose MED than did those under 40 (15 vs. 4%, $p < 0.05$). Additionally, a larger percentage of patients with a pain diagnosis received a high MED than patients without a pain diagnosis (18 vs. 8%, $p < 0.001$). Neither viral suppression nor CD4 count was associated with high MED or long-term opioid prescriptions.

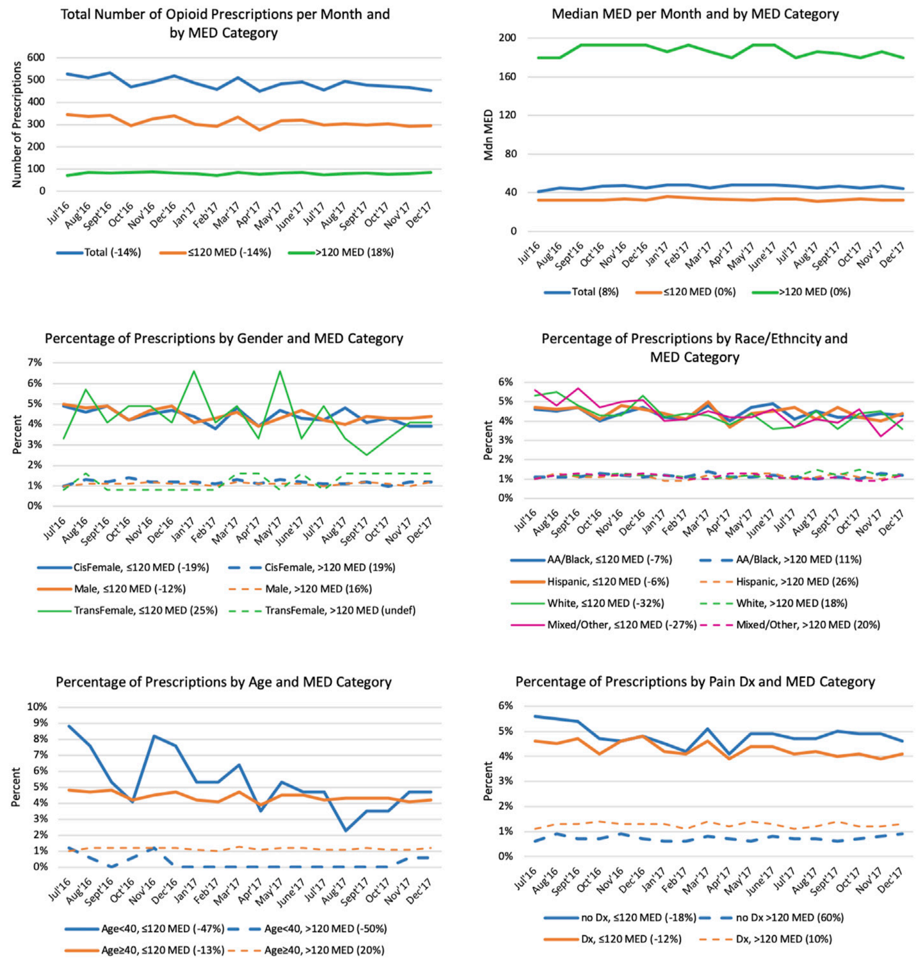
Multivariate Analyses

Separate multivariate analyses examined which factors were independently associated with either receipt of any opioid prescription, receipt of high MED, or VL nonsuppression (**Table 2**). Logistic regression controlling for age group, gender, race/ethnicity, and years since HIV diagnosis showed that the presence of pain diagnosis, OUD and mental health disorders were independently associated with receipt of any opioid prescription. Among patients with prescriptions, adjusted logistic regression examining MED indicated increased odds of a chronic high-dose prescription among patients with pain diagnoses compared to patients without those diagnoses. The last model examined viral suppression and found that SUD increased the likelihood of detectable VL after accounting for demographic and clinical factors. Having a chronic high MED was not found to be independently associated with having a detectable VL when compared to those who were not prescribed opioids and those with low MED opioid prescriptions.

DISCUSSION

We characterized trends in opioid prescription patterns among patients receiving HIV care over 18 months following the publication of the 2016 CDC pain management guidelines, identified risk factors for chronic high risk opioid prescriptions, and examined the impact of prescriptions on virologic suppression. Of the 8,882 patients receiving HIV care, 12% had at least one opioid prescription during the study period, which was lower than estimates of between 17 to 53% found in prior studies (Silverberg et al., 2012; Edelman et al., 2013; Koeppe et al., 2013; Jeevanjee et al., 2014; Merlin et al., 2016; Canan et al., 2018; Flores et al., 2018; Canan et al., 2019; Edelman et al., 2020). During the study, the majority (56%) of patients with an opioid prescription received 1-3 prescriptions and 40% received long-term (>365 days) prescriptions. In adjusted analysis, the presence of pain diagnosis, OUD and mental health disorders were independently associated with an increased likelihood of having received at least one opioid prescription. Overall, the number of monthly prescriptions decreased by 14% from the first month to the last month of the 18-month period, and this decrease occurred primarily among low MED prescriptions, which represented most (80%) of the prescriptions during the study. However, a 18% increase was observed in receipt of chronic high dose prescriptions (>120 MED), representing about 20% of prescriptions during the study. Taken together, these data suggest that public health guidelines and regulations that directly address prescribing practices can have an impact in reducing the overall number of prescriptions, at least in the immediate short-term, but additional approaches may be needed to specifically address initiation of high MED and transitions from low to high dose and high risk prescriptions.

Among patients receiving any opioid prescriptions, chronic high risk opioid prescriptions were provided to 14% of those with available MED data, which is similar to Merlin et al.'s estimate of 17% of patients with chronic prescriptions, (Merlin et al., 2016),



Note. ªPercentages presented in the legend of each chart represent the change in the number of opioid prescriptions between July 2016 (x) and December 2017 (y), which were calculated as (y-x)/x for each subgroup.

FIGURE 1 | Monthly Opioid Prescriptions and Average Daily Morphine Equivalent Dose (MED) Trajectories by Patient Demographic and Clinical Characteristics[a]. Note. [a]Percentages presented in the legend of each chart represent the change in the number of opioid prescriptions between July 2016 (x) and December 2017 (y), which were calculated as (y–x)/x for each subgroup.

but higher than estimates in earlier studies (between 6-10%) (Silverberg et al., 2012; Edelman et al., 2013). However, using four separate indicators for high risk opioid prescriptions based on national criteria for prescription monitoring, Canan and colleagues found that 30%, a substantial larger percentage of PWH compared to our finding (14%), met criteria for high risk opioid prescriptions (Canan et al., 2018). In our study, only pain diagnoses were found to predict high MED prescriptions in adjusted logistic regression analysis. The likelihood of chronic high risk opioid prescriptions was elevated in patients with pain diagnoses compared to patients without those diagnoses. Our findings are similar to those found in the study conducted by Canan and colleagues (2018), which found that pain diagnoses were associated with high risk prescriptions but no associations between high risk prescriptions and other factors, such as mental health disorders or viral suppression (Canan et al., 2018). Importantly, in our study, having documentation of SUD, not including OUD, was predictive of viral nonsuppression, after controlling for all other variables in the model. Both receipt of an opioid prescription and receipt of a high MED prescription were not significantly associated with viral suppression. A similar percentage of patients with suppressed and nonsuppressed VL were likely to receive any opioid prescription or high MED prescriptions. In contrast to our findings, Flores et al. found that virologic failure was more likely among patients receiving any opioid prescription, after accounting for known predictors of high VL (Flores et al., 2018).

These findings have important implications for the prevention of chronic high risk prescriptions in the clinical care of PWH with comorbid conditions, including pain-related, mental health and substance use disorders. It is important to note that EMR documentation of recent substance use during a primary care visit was made for only about 30% of patients and thus, recent substance use may be underestimated. This issue has been found

TABLE 2 | Unadjusted and Adjusted Logistic Regression Analyses of Factors Associated with Receipt of Opioid Prescription, High average daily morphine equivalent dose (MED) Prescription, and with Unsuppressed HIV Viral Load.

	Any opioid prescription		**High MED opioid prescription**		**Unsuppressed HIV viral load**	
	Unadjusted (*n* = 8,882)	**Adjusted (*n* = 6,579)[a]**	**Unadjusted (*n* = 772)**	**Adjusted (*n* = 570)[b]**	**Unadjusted (*n* = 8,746)**	**Adjusted (*n* = 6,302)[a]**
	OR (95% CI)	**AOR (95% CI)**	**OR (95% CI)**	**AOR (95% CI)**	**OR**	**AOR (95% CI)**
Age <40 years	0.29 (0.24–0.35)***	0.49 (0.38–0.64)***	0.21 (0.05–0.86)*	0.16 (0.02–1.31)	1.15 (1.02–1.28)*	1.14 (0.97–1.34)
Gender						
Male[c]	0.46 (0.40–0.53)***	0.54 (0.46–0.64)***	0.90 (0.59–1.38)	1.25 (0.72–2.14)	0.76 (0.67–0.86)***	0.88 (0.76–1.03)
Transgender female	1.66 (0.95–2.88)	2.05 (1.01–4.16)*	1.73 (0.46–6.57)	4.45 (0.96–20.59)	0.91 (0.50–1.65)	0.93 (0.45–1.94)
Cisgender female	Ref	Ref	Ref	Ref	Ref	Ref
Ethnicity/Race						
African-american	1.42 (1.18–1.72)***	1.12 (0.89–1.41)	1.27 (0.69–2.35)	1.69 (0.75–3.83)	2.25 (1.92–2.63)***	2.14 (1.78–2.58)***
Hispanic	1.75 (1.44–2.13)***	1.19 (0.94–1.51)	1.00 (0.53–1.90)	1.31 (0.56–3.06)	1.30 (1.09–1.55)**	1.24 (1.00–1.53)*
Other/Multiple	0.96 (0.77–1.20)	0.85 (0.65–1.11)	1.08 (0.51–2.27)	1.51 (0.58–3.96)	1.65 (1.38–1.97)***	1.62 (1.32–2.00)***
White	Ref	Ref	Ref	Ref	Ref	Ref
Years since HIV diagnosis						
<5 years	0.35 (0.28–0.43)***	0.69 (0.54–0.87)**	0.95 (0.46–1.95)	1.49 (0.69–3.24)	1.15 (1.00–1.33)*	1.14 (0.96–1.34)
5 < 10 years	0.67 (0.55–0.81)***	0.80 (0.65–0.98)*	0.53 (0.24–1.14)	0.58 (0.26–1.27)	1.02 (0.87–1.19)	1.02 (0.86–1.21)
≥10 years	Ref	Ref	Ref	Ref	Ref	
Pain diagnosis	4.41 (3.86–5.05)***	3.36 (2.85–3.95)***	2.63 (1.59–4.34)***	2.49 (1.35–4.62)**	0.95 (0.85–1.07)	0.89 (0.77–1.04)
SUD (excluding OUD)	1.41 (1.19–1.65)***	1.07 (0.87–1.31)	0.82 (0.49–1.37)	0.67 (0.34–1.30)	1.72 (1.51–1.96)***	1.79 (1.52–2.11)***
OUD	2.97 (2.34–3.78)***	2.22 (1.63–3.01)***	1.11 (0.59–2.09)	1.14 (0.53–2.48)	1.41 (1.10–1.79)**	1.31 (0.96–1.80)
Mental health disorder	1.74 (1.53–1.99)***	1.31 (1.11–1.54)**	1.05 (0.70–1.57)	1.20 (0.70–2.04)	1.06 (0.95–1.19)	0.98 (0.86–1.13)
MED						
No opioid prescription	-	-	-	-	0.68 (0.44–1.05)	0.67 (0.39–1.15)
Low MED	-	-	-	-	0.75 (0.47–1.20)	0.72 (0.41–2.29)
High MED					Ref	Ref

[a] *Excludes patients with missing data mostly due to missing HIV diagnosis date.*

[b] *Excludes patients with missing MED data and HIV diagnosis date.*

[c] *Includes 6,843 cisgender and 3 transgender males.*

$*p < .05$; $**p < .01$; $***p < .001$

SUD = substance use disorder; OUD = opioid use disorder; MED = average daily morphine equivalent dose; OR = odds ratio; AOR = adjusted odds ratio.

in prior studies; documentation was unavailable for 37% of patients who received opioid prescriptions in the study conducted by Flores and colleagues (Flores et al., 2018). While the identified gaps in substance use screening is an important finding, indicating the need for effective strategies to enhance substance use screening rates, EMR are key to facilitate the integration of services for substance use within HIV primary care (Tai et al., 2012; Ghitza et al., 2013).

One set of important interventions has been the development and dissemination of opioid prescribing guidelines and pain management strategies which emphasize that non-pharmacologic interventions, and non-opioid pharmacologic interventions should be considered first line, to reduce risk for complications of opioid use among PWH (Bruce et al., 2017; Flores et al., 2018). Qualitative studies focusing on the training needs of HIV treatment providers, such as the study conducted by Starrels and colleagues (Starrels et al., 2016) could help in the development of interventions and programs to enhance the implementation of and adherence to evidence-based practices grounded in consensus opioid prescribing and pain management guidelines. Several efforts are currently underway to improve knowledge and training about pain management, co-occurring mental health and SUD, and pharmacotherapy, as well as to facilitate screening, monitoring and judicious prescribing among HIV primary care providers (Lum et al., 2011; Bruce et al., 2017). Robinson-Papp and colleagues developed an innovative intervention, TOWard SafER Opioid Prescribing (TOWER), (Robinson-Papp et al., 2019), to support providers in applying CDC's guidelines with their patients by providing tools in the management of pain and opioid prescribing practice. Patients use an SMS-based app daily to record pain intensity and benefits of treatment, adverse reactions and harms, and non-pharmacologic treatment and opioid use in order to provide data for a risk-benefit assessment. Patient's responses, along with EMR and records from prescription monitoring programs are summarized in an app that providers use to support patients managing their pain. Focusing on chronic opioid use and HIV treatment, Lira and colleagues developed the Targeting Effective Analgesia in Clinics for HIV (TEACH) intervention to support providers by providing access to a specialized nurse care manager, an addiction specialist, and prescriber education and training (Lira et al., 2019). Other educational efforts are already proving to have an effect in improving knowledge among providers about prescribing guidelines in NYC regarding acute pain, chronic noncancer pain, and the dangers of high-dose opioid prescriptions (Kattan et al., 2016).

Limitations

This study has important limitations which need to be considered. First, although this study was based on large retrospective dataset over an 18-month period, we aggregated individual prescriptions for each patient, and therefore, we did not conduct analyses to make any causal inferences. While we were able to determine associations between individual demographic and clinical indicators and opioid prescriptions, observational studies cannot demonstrate causation and therefore, associations should be interpreted with caution. Second, there are inherent limitations to EMR data because they are dependent on documentation of the clinical encounter, prescriptions made, and whether patients are asked about or report symptoms or problems beyond their immediate HIV care needs. As noted above documentation of recent substance use during a primary care visit was made for only about 30% of patients and thus, recent substance use may be underestimated. Additionally, reliance on ICD diagnostic codes to define the various disorders has limitations as some conditions may be undiagnosed or otherwise not recorded, including pain diagnoses. Furthermore, because we could not readily determine from the extracted EMR whether methadone and buprenorphine were prescribed to treat pain vs. to treat opioid use disorders, we excluded records of patients receiving methadone or buprenorphine. Third, we did not interview or conduct any assessments with patients. Although bias related to recall and social desirability is introduced with self-reports, we could not assess whether the opioid prescriptions documented in EMR were dispensed by the pharmacy, if patients complied with doctor's orders and took them as prescribed, or whether additional opioid prescriptions were dispensed by providers outside the healthcare system in this study. The results of this study may not generalizable to PWH not retained in HIV care, and given that a large percentage of patients in our sample were virally suppressed, the results may also not be generalizable to all PWH in HIV care. We were also limited in the records that were attained from EMR system and could not follow up directly with patients to fully obtain the diversity of the sample of patients. This limitation is most apparent in our approach of collapsing the gender identity variable. Additionally, EMR included in this study were not from a nationally representative sample of patients; however, the sample was very diverse in terms of gender and race/ethnicity.

CONCLUSION

Our findings show that receipt of opioid prescriptions, including high MED, and therefore potentially high risk, opioid prescriptions, including receipt of prescriptions for long durations, are common among PLW who are in care. Despite large-scale efforts to improve prescribing guidelines and implement monitoring systems, additional efforts are needed for PWH to support patients and clinicians in reducing chronic high risk use of prescription opioids, particularly for patients with co-occurring pain-related, mental health and substance use disorders. More recently, the NIH has advanced an initiative called Helping to End Addiction Long-term (HEAL) for addiction and pain research to treatments for problematic opioid use and pain (see www.heal.nih.gov) (Collins et al., 2018) Examination of trends in prescribing patterns and identification of factors that impact the course of opioid use among PWH are crucial, particularly given their potential to identify both, trajectories that move beyond use and misuse to OUD, and prevention and treatment targets within healthcare systems. Future research is needed to better characterize transitions to chronic high risk use to inform pain management and opioid prescribing practices for patients receiving HIV care to simultaneously improve pain management, to optimize HIV outcomes including viral suppression, and to reduce the risks of prescription opioid use.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Program for the Protection of Human Subjects (PPHS) at the Icahn School of Medicine at Mount Sinai (ISMMS). Written informed consent for participation was not required for this study in accordance with institutional requirements.

AUTHOR CONTRIBUTIONS

All authors contributed to drafting and revising the manuscript and final approval of the submitted version. All authors contributed to the design of the study (AV, GH, EF, BAD, ST, BL, JG, DC, JR, JAA, DCP) and/or acquisition and processing of data (AV, GH, EF, BAD, ST, BL, JG) and/or analysis of data (AV, JAA, DCP).

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A Vulnerability Assessment for a Future HIV Outbreak Associated With Injection Drug Use in Illinois, 2017–2018

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The current opioid crisis and the increase in injection drug use (IDU) have led to outbreaks of HIV in communities across the country. These outbreaks have prompted country and statewide examination into identifying factors to determine areas at risk of a future HIV outbreak. Based on methodology used in a prior nationwide county-level analysis by the US Centers for Disease Control and Prevention (CDC), we examined Illinois at the ZIP code level ($n = 1{,}383$). Combined acute and chronic hepatitis C virus (HCV) infection among persons <40 years of age was used as an outcome proxy measure for IDU. Local and statewide data sources were used to identify variables that are potentially predictive of high risk for HIV/HCV transmission that fell within three main groups: health outcomes, access/resources, and the social/economic/physical environment. A multivariable negative binomial regression was performed with population as an offset. The vulnerability score for each ZIP code was created using the final regression model that consisted of 11 factors, six risk factors, and five protective factors. ZIP codes identified with the highest vulnerability ranking (top 10%) were distributed across the state yet focused in the rural southern region. The most populous county, Cook County, had only one vulnerable ZIP code. This analysis reveals more areas vulnerable to future outbreaks compared to past national analyses and provides more precise indications of vulnerability at the ZIP code level. The ability to assess the risk at sub-county level allows local jurisdictions to more finely tune surveillance and preventive measures and target activities in these high-risk areas. The final model contained a mix of protective and risk factors revealing a heightened level of complexity underlying the relationship between characteristics that impact HCV risk. Following this analysis, Illinois prioritized recommendations to include increasing access to harm reduction services, specifically sterile syringe services, naloxone access, infectious disease screening and increased linkage to care for HCV and opioid use disorder.

Keywords: injection drug abuse, HIV, vulnerability analysis, outbreak, infectious disease, hepatitis C (HCV) infection

INTRODUCTION

HIV outbreaks related to injection drug use (IDU) in the setting of the current opioid crisis have been reported in communities across the U.S. In 2014, Scott County, Indiana identified more than 200 cases of HIV linked to the injection of prescription opioids. In subsequent years Massachusetts identified an outbreak of 116 cases with HIV that occurred among people who inject drugs (PWID)[1] (Alpren et al., 2020), and more recently, West Virginia has experienced HIV clusters amongst the PWID communities in multiple counties[2],[3]. Outbreaks of HIV have also been associated with underlying and preceding networks of hepatitis C virus (HCV) infection, which may portend future risk of HIV given the relationship with drug injection (Shepard et al., 2005; Mumtaz et al., 2015; Ramachandran et al., 2018).

The opioid crisis, which has disproportionately affected rural communities has laid bare the multiple population and environmental factors that underlay vulnerability to these infectious diseases (Keyes et al., 2014; Van Handel et al., 2016). Individual-level characteristics, such as demographic (e.g., age, race, and disability status) and socioeconomic factors (i.e., poverty status, employment, homelessness, and education) are associated with risk of HIV (Des Jarlais et al., 2020; Schalkoff et al., 2020). Low healthcare access, including infectious disease screening, prevention measures, such as syringe service programs and substance use disorder treatment can affect the spread of a disease related to injection drug use (Havens et al., 2018; Lerner and Fauci, 2019; McLuckie et al., 2019; Siegler et al., 2019). At the level of the physical environment, characteristics, such as transportation and types of housing can impact engagement in and utilization of HIV services[4] (Aidala et al., 2016). In Illinois, fatal and nonfatal overdoses related to opioids have increased by 3% between 2018 and 2019[5]. While the major metropolitan areas have represented the majority of absolute cases, rural areas have experienced some of the highest per population rates of both overdose as well as other consequences of the opioid epidemic, such as neonatal abstinence syndrome[6],[7]. HCV infection in the state has increased by 43% from 6,887 in 2006 to 9,838 in 2017, with many of the cases in individuals younger than 35 years of age and linked to injection drug use[8].

Prior studies, including analyses performed by the Centers for Disease Control and Prevention (CDC) have examined multiple factors at the national level to identify areas at high risk of rapid HIV transmission (Rickles et al., 2018; McLuckie et al., 2019). Such work has outlined a methodological model for vulnerability analysis that has inspired states to take a finer approach in examining factors based on local data.

We offer further insight at the subcounty, ZIP code level in Illinois to what local areas are vulnerable to an HIV outbreak. Recent work in southern Illinois showed more variation at the ZIP-scale than the county-level, necessitating further investigation at the full state scale (McLuckie et al., 2019). ZIP code-level analysis provides a more granular understanding of risk within large and diverse counties in Illinois, but is also generally large enough to protect individual privacy when summarizing health records. This may allow local jurisdictions to more narrowly target specific public health interventions within these vulnerable areas in an effort to prevent future outbreaks. Additional inclusion of environmental factors will provide further contextual information to identify resource gaps that may impact outbreak risk.

MATERIALS AND METHODS

Study Design

An ecologic study design was used to evaluate associations of HCV health outcomes and various related health outcomes, treatments, intervention, and risk factors at an environmental scale. ZIP code tabulation (ZCTA) level indicators were collected from the 2013–2017 five-year average US Census American Community Survey, Illinois state-specific indicators from the CDC, and surveillance data related to HCV, sexually transmitted diseases and fatal and non-fatal opioid-related overdose from the Illinois Department of Public Health. Data were collected for 2017 and 2018 to mirror the methodology used by CDC (Van Handel et al., 2016). Illinois' 1,383 ZCTA codes comprised the study sample. Covariates were collected and analyses conducted at the ZIP code level.

Data

ZIP code level vulnerability to an HIV or HCV outbreak related to injection drug use was indicated by the detection incidence of HCV cases from 2017 to 2018. All confirmed and probable cases of HCV infection (chronic and acute) in individuals <40 years of age were included (**Table 1**). This designation was used as a proxy for acute HCV infections which are known to be underreported due to the asymptomatic and minimally symptomatic nature of most acute infections (Onofrey et al., 2015). HCV detection incidence was defined as diagnosed cases meeting a confirmed case definition for HCV infection, indicated by a positive HCV nucleic acid test or HCV antigen test. Rates were obtained from the Illinois Department of Public

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Health (IDPH) program and the Illinois- National Electronic Disease Surveillance System (I-NEDSS), which collects mandated infectious disease reporting from laboratories, health care providers, and other mandatory reporters.

ZIP code level predictors were identified through author consensus as potentially predictive of high risk for HIV/HCV transmission and summarized across all Illinois ZCTA areas ($n = 1383$). Some indicators were collected as counts and subsequently calculated as rates, per total population between ages 15–40 years (**Table 1**).

Chlamydia, gonorrhea and syphilis cases were collected *via* the same mechanism as HCV. Fatal overdose rates were extracted from Illinois Vital Records: heroin deaths were assigned as any drug overdose death in which heroin (ICD-10 code T40.1) was reported as a cause of death; analgesic deaths were assigned as any drug overdose death in which prescription analgesics (methadone, synthetic narcotics, or other prescription opioids, ICD-10 codes T40.2, T40.3, T40.4) were reported as a cause of death; opioid deaths as any drug overdose death in which any opioid drug was a contributing cause of death—includes the above four ICD-10 codes as well as T40.0 (opium) and T40.6 (other/unspecific narcotics). Non-fatal opioid-related overdose rates were collected from IDPH hospital and emergency department (ED) discharge data.

To better understand access to resources throughout the state, we included several treatment and intervention variables: 1) access to a pharmacy utilizing a naloxone standing order; 2) access to clinicians or clinics that can prescribe/dispense buprenorphine, methadone, or naltrexone; 3) and access to federally qualified health centers (FQHC). These systems were included within access to resources due to their ability to serve and engage the community (Joudrey et al., 2019). Specifically, FQHC's serve medically underserved areas, provide a wide range of services, including counseling and medication-assisted treatment, and have been shown to be associated with opioid-related mortality (Haley et al., 2019; Flores et al., 2020). Access to pharmacies with a standing order for naloxone (from the IDPH registry), "drug use disorder treatment programs" (as defined by methadone outpatient treatment clinics), buprenorphine-waivered physicians with records of prescribing in the Illinois Prescription Monitoring Program, and naltrexone providers (sourced from the Substance Abuse and Mental Health Services Administration 2018 dataset), and federally qualified health centers (from study collection) were available as locations at the address level, and subsequently geocoded and converted to spatial data points. Distance from the ZIP code center to nearest facility was then calculated in QGIS software.

ZIP code level demographics were collected from the American Community Survey 2013–2017, five-year estimate (American Community Survey 2017). Covariates reflect place-based features of the Risk Environment Model that guide studies of the social determinants of HIV-related outcomes among PWID, recently extended and adapted to southern Illinois at the ZCTA scale (Rhodes, 2009; Kolak et al., 2020). Covariates were extracted to approximate varying dimensions of risk across social, economic, and physical environments as guided by review of the Risk Environment Model literature, as well as input from local and state-level taskforce meetings involving stakeholders from local health departments, emergency medical services and other first responders, community-based service organizations. and advocacy groups. Percent Whites, Blacks, and Hispanic persons were included at the ZIP code level (Keyes et al., 2014). Seniors were designated by percent of population over 64 years of age, young adults by percent of population aged 15–24 years, and percentage of persons with a disability (Keyes et al., 2014). Areas with greater proportions of seniors, young adults, and/ or persons with a disability may reflect different dimensions of neighborhood structures that can influence, interact with, and impact opioid use disorder (OUD) risk environments (Brady et al., 2017). Also included were indicators of socioeconomic status including percent of households in poverty, per capita income; percent unemployment; percent of working aged individuals without a high school diploma; and an income inequality Gini coefficient. Income was normalized for interpretability through a log transformation. "High risk" employment was proxied as the percent of individuals employed in agricultural, forestry, mining, logistics/utilities, construction, and manufacturing industries; these jobs were identified as at a greater risk of injury according to the CDC. Furthermore, variables were included that may act as physical environment indicators such as proportion of mobile homes, percent of vacant homes, percent persons who have lived in their home for more than 20 years, and percent renters (Kolak et al., 2020).

Regression

Given the large sample size ($n = 1383$) due to using the ZIP code level approach, the number of indicators did not need to be reduced for analysis. Each variable was independently assessed for association with the outcome. To assess correlation between indicators, we developed a Spearman correlation matrix. The correlation matrix was calculated for pairwise complete observations and correlation plot was implemented with the proc corr package in SAS version 9.4 software (SAS Institute, Cary, North Carolina).

A multivariable negative binomial regression was performed for all five-digit ZIP code tabulation areas in Illinois, with ZCTA code level population as an offset. Negative binomial regression allowed for adjusting of the model variance independently of the mean compared to Poisson. Social, economic, and physical environment variables were included in the model based on a-priori hypotheses (Kolak et al., 2020). The goal was to create a parsimonious model, retaining variables only at the $p \leq 0.05$ level. Backwards stepwise deletion was performed. Following each regression, the most non-significant variable was removed individually. This step was then repeated until all predictors were significant at $p \leq 0.05$.

Vulnerability Score and Ranking

The vulnerability score was developed using the final regression model. The coefficient of each significant indicator was used to compute each ZIP code's index score. This score was the predicted count value at the ZIP code level. This score was then converted to a rate by dividing twice the 2017 population since counts were from 2017 and 2018. This predicted rate value was then used to rank ZIP codes from highest to lowest, where higher scores indicated increased vulnerability. The top 10% of ZIP codes were designated as "most vulnerable" and the next 10% of ZIP codes were designated as "very vulnerable."

RESULTS

All covariates were assessed for correlation. Individual rates of chlamydia, syphilis and gonorrhea were strongly correlated (>0.90). One variable was created as an overall sexually transmitted infection rate by summing values for the number of cases of chlamydia, syphilis and gonorrhea. All other predictors were not significantly correlated (<0.65) and therefore included in the model. The remaining predictors were used to model HCV infection in those under 40 years of age as a proxy for an HIV/ HCV outbreak. Vacant housing was excluded due to not being associated with HCV infection.

An association was observed between 11 covariates and HCV detection incidence [χ^2 $(1358, N = 1370) = 1238.71, p \leq 0.001$]. Of these, one was health related: (1) overdose risk (fatal and nonfatal) (estimate, 0.024; $P \leq 0.0001$) (**Table 2**). Five variables reflected social characteristics across ZCTAs: (1) percentage White (estimate, 0.015; $P \leq 0.0001$); (2) percentage Hispanic (estimate, −0.009; $P \leq 0.0001$); (3) percentage over 65 years of age (estimate, −0.018; $P = 0.018$); (4) percentage disabled (estimate, 0.038; $P \leq 0.0001$) and (5) percentage 15 to 24 years of age (estimate, −0.014; $P = 0.032$). Three of the indicators were economic: (1) poverty rate (estimate, 0.016; $P = 0.008$); (2) log of per capita income (estimate, −1.059; $P = 0.002$); and (3) risky jobs (estimate, −0.009, $P = 0.031$). Two variables were physical environment indicators: (1) mobile home (estimate, 0.028; $P < 0.0001$) and (2) rental housing (estimate, 0.015; $P < 0.0001$).

When using our vulnerability ranking, the ZIP codes with highest vulnerability were found to be distributed across the state yet focused in the rural southern region (**Figure 1**). Ten counties in the more populated northern region of the state had at least one vulnerable ZIP code. Only one vulnerable ZIP code was in highly urbanized Cook County. Among the central region of the state, a group of vulnerable ZIP codes appeared around the third largest urban area in the state, the city of Peoria, in Peoria and Tazewell counties. Two rural counties in the western/ central region of the state, Mason and Greene counties, also had groupings of vulnerable ZIP codes. Two rural counties in the eastern region of the state, Iroquois and Ford counties, had a few vulnerable ZIP codes. Two counties in the southern, central region of the state were almost fully identified as vulnerable through their ZIP codes (Franklin and Saline County). Hardin counties, a southeastern rural county and the only Illinois, county identified by in the CDC analysis had two vulnerable ZIP codes.

DISCUSSION

We identified communities at the ZIP code level across Illinois vulnerable to an injection drug use-related HIV outbreak using statewide data sources from 2017–2018. Our finer-scaled analysis illustrated more vulnerable regions compared to the national view, providing more precise indications of vulnerability below county scale. The CDC identified one county, Hardin County, as highest risk through their assessment (Van Handel et al., 2016). This county is the least populous county in rural, southern Illinois and shares a border with Kentucky. Out of the four ZIP codes within this county, our study found that two were of the most vulnerable ZIP codes in the entire state of Illinois. We furthermore refined our understanding of HCV detection incidence in Illinois with an extended review of multiple risk factors. Areas with more Hispanic residents, seniors, college-aged students, persons employed in "high risk jobs," and/or higher incomes were associated with decreased HCV detection incidence, whereas the remaining covariates (opioid-related overdose, areas with more White residents, persons with a disability, mobile home structures, and/or greater proportion of rental housing) were associated with increased incidence.

Illinois has often been referred to as a microcosm of the country, being representative of the national demographics related to age, race, education, and household income. While Chicago is the third most populous city in the US, nearly two-thirds of the state's 102 counties are rural. Disparities between large metropolitan and rural areas exist for a broad swath of health outcomes much as they do nationwide. While absolute cases of chronic HCV are correlated with higher population density, acute HCV incidence in the US has been increasing with a greater predominance in rural counties in association with the opioid epidemic (Zibbell et al., 2018). Consistent with these national trends and other published vulnerability analyses, ZIP codes of high risk were clustered in rural Illinois (Wesner et al., 2020). At the same time, regions of heightened vulnerability in southern Illinois identified in previous work persist in this analysis, but are put into context within the wider state's landscape (McLuckie et al., 2019). While the spread of HIV in the country is primarily driven by sexual transmission, in non-metropolitan settings injection drug use contributes to higher rates of new diagnoses as compared to urban areas (Schranz et al., 2018). These risks are also reflected in Illinois where the rate of opioid overdose increase disproportionately burdens rural counties and were identified as the significant health-related predictor in this regression model. Factors such as limited access to OUD, HIV and HCV treatment in rural settings may contribute to worse health outcomes and increased risk[9] (Illinois Department of Public Health, 2017; McLuckie et al., 2019).

Prior analyses of Illinois public health surveillance data have demonstrated other demographic variables associated with

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[9] Neonatal Abstinence Syndrome Advisory Committee and Illinois Department of Public Health (2019). Available online at: https://dph.illinois.gov/sites/default/files/publications/nas-annual-report-march-2019.pdf

TABLE 1 | Dependent variable and indicators originally identified to be used in regression model at the ZIP code level, Illinois, 2017–2018.

	Definition	Source
Health Outcomes		
1. Acute and chronic HCV cases under the age of 40 years (dependent variable)	Number of confirmed HCV cases	Illinois Department of Public Health[a]
2. Chlamydia	Number of confirmed chlamydia cases	
3. Syphilis	Number of confirmed syphilis cases	
4. Gonorrhea	Number of confirmed gonorrhea cases	
5. Fatal and non-fatal opioid-related overdose*	Combined number of nonfatal and fatal opioid- related overdose	Hospital Discharge Data and Vital Statistics[b,c]
Access/resources		
6. Naloxone access	Pharmacy or Opioid Education and Naloxone Distribution Program utilizing the statewide Naloxone Standardized Procedure	Illinois Department of Public Health[d]
7. Federally Qualified Health Centers	Location of Federally Qualified Health Centers as of January 1, 2019	Health Resource and Services Administration Data Portal[e]
8. Drug and alcohol use disorder treatment programs	Methadone outpatient treatment clinics	Substance Abuse and Mental Health Services Administration 2018 dataset[f]
9. Drug and alcohol use disorder treatment programs	Buprenorphine-waivered physicians	Substance Abuse and Mental Health Services Administration 2018 dataset (see text footnote *f*)
10. Drug and alcohol use disorder treatment programs	Naltrexone providers	Substance Abuse and Mental Health Services Administration 2018 dataset (see text footnote *f*)
Social, Economic, and Physical Environment		
11. Black %	Percent of persons who reported they were not Hispanic or Latino and were of Black race.	United States Census Bureau. American Community Survey 2013–2017. Five-year estimates[g]
12. White %*	Percent of persons who reported they were not Hispanic or Latino and were of White race alone.	
13. Hispanic %*	Percent of persons who reported they were Hispanic or Latino.	
14. Over 65*	Percent of persons who reported they were over 65 years of age.	
15. Population 15–24*	Percent of persons who reported they were between 15 and 24 years of age.	
16. Disability rate*	Percent of persons who reported they were disabled.	
17. Poverty rate*	Percent of persons in poverty according to levels defined by the Census Bureau, which uses a set of income thresholds that vary by family size and composition to determine who is in poverty. If a family's total income is less that the family's threshold, then that family and every individual in it is considered in poverty.	
18. Income*	Mean income per person in the county; derived by dividing the total income of all people 15 years and older by the total population; modeled as $\log_{10.}$	
19. Unemployment rate	Number of civilian persons unemployed and actively seeking work divided by the estimated total civilian population aged 16yrs and older.	
20. Education	Number of persons aged 25 yrs or older with less than a 12 grades education (including individuals with 12th grade, but no diploma) divided by the estimated ZIP code level population aged 25 yrs and older).	
21. Gini Index	Measure of the distribution of income across income percentiles in the population.	
22. Risky jobs*	Percent individuals employed in agricultural, forestry, mining, logistics/utilities, construction, and manufacturing industries.	

(Continued)

TABLE 1 | Continued

	Definition	Source
23. Mobile home*	Percent mobile home structures	
24. Vacant home	Proportion of vacant to occupied homes	
25. Rental house*	Percent renters	
26. Old home	Percent of persons who have lived in their home for more than 20 years.	

[a] *Illinois Department of Public Health. Infectious Disease Reporting. Available online at: http://www.dph.illinois.gov/topics-services/diseases-and-conditions/infectious-diseases/infectious-disease-reporting.*

[b] *Illinois Department of Public Health. Death Statistics. Available online at: http://www.dph.illinois.gov/data-statistics/vital-statistics/death-statistics/more-statistics.*

[c] *Illinois Department of Public Health. Discharge Data. Available online at: http://dph.illinois.gov/topics-services/prevention-wellness/patient-safety-quality/discharge-Data.*

[d] *Illinois Department of Human Services. IDHS/SUPR Initiatives in Response to the Opioid Crisis. Available online: http://www.dhs.state.il.us/page.aspx?item=105980.*

[e] *Health Resource and Services Administration. Data Portal. Available online at: https://data.hrsa.gov/hdw/tools/dataportal.aspx.*

[f] *Substance Abuse and Mental Health Services Administration. Legislation, Regulations, and Guidelines. Available online at: https://www.samhsa.gov/programs-campaigns/medication-assisted-treatment/legislation-regulations-guidelines.*

[g] *United States Census Bureau. Available online at: https://www.census.gov/data/datasets/2017/demo/popest/counties-total.html.*

**Final variable in model.*

TABLE 2 | Negative binomial regression results for final model with significant indicators.

Parameter	Coefficient	Standard Error	*P*-value
Intercept	−5.94	1.62	0.0002
Overdose risk	0.024	0.005	<0.0001
Percentage White	0.015	0.002	<0.0001
Percentage Hispanic	−0.009	0.002	<0.0001
Percentage over 65 years	−0.018	0.008	0.018
Percentage population 15–24 years	−0.014	0.007	0.032
Percentage disabled	0.038	0.009	<0.0001
Percentage poverty	0.016	0.006	0.008
Log income	−1.059	0.334	0.002
Percentage in a risky job	−0.009	0.004	0.031
Percentage mobile home	0.028	0.005	<0.0001
Percentage rental housing	0.015	0.003	<0.0001

increased risk of HCV, including white race, 25–64 age group and residence in rural counties (Jones et al., 2017). In contrast to a jurisdictional vulnerability analysis performed for South Dakota where disability was noted to be protective, in our analysis self-reported disability was associated with increased vulnerability to HCV. Given the complex association of disability with substance use disorder and that both overdose-related hospitalizations and mortality have been shown to be disproportionately represented in Medicare-disability beneficiaries, our findings are plausible and suggest that this population may benefit from focused preventive interventions (Compton et al., 2007; Glazier and Kling, 2013; Peters et al., 2018; Kuo et al., 2019).

Higher income and lower percentage in poverty were protective factors, consistent with prior vulnerability analyses (Van Handel et al., 2016; Rickles et al., 2018; Sharareh et al., 2020). Risky jobs, characterized as employment in the agricultural, forestry, mining, logistics/utilities, construction, and manufacturing industries are more prevalent in non-urban Illinois[10]. While high risk employment may be prone to work-related injury and potentially increased utilization of prescription opioids, we found the proportion of such jobs to be protective at a ZIP code level. This may be due to the higher income and employment benefits. However, in a regional analysis we previously identified southern regions of the state with a high proportion of high-risk jobs that correlated with increased opioid-related overdose prevalence, suggesting a spatially heterogeneous effect (Kolak et al., 2020). Additionally, during the timeframe of the analysis employment in the agricultural, mining and logging, manufacturing, and construction industries were stable or increasing in the state[11]. It is possible that factors, such as job stability/growth and non-payroll incentives or benefits may be mediating factors. Further research is warranted to better understand the dynamics around degrees of rurality, high risk employment, and other structural benefits not reflected in per capita income in relation to disease risk.

The percentage of mobile homes and rental housing were independently associated with HCV risk suggesting that some

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[10] Illinois Institute for Rural Affairs. *A Snapshot of Rural Illinois. Investing in Healthy Rural Communities: Harvesting the Power of People, Place, and Partnerships*. Available online at: http://www.rwhc.com/mediasite/6-App-Chris%20Merrett_Plenary%20am.pdf

[11] Bureau of Labor Statistics. *BLS Data Finder*. Available online at: https://beta.bls.gov/dataQuery/find?fq=survey:%5Bsm%5Dands=popularity:D

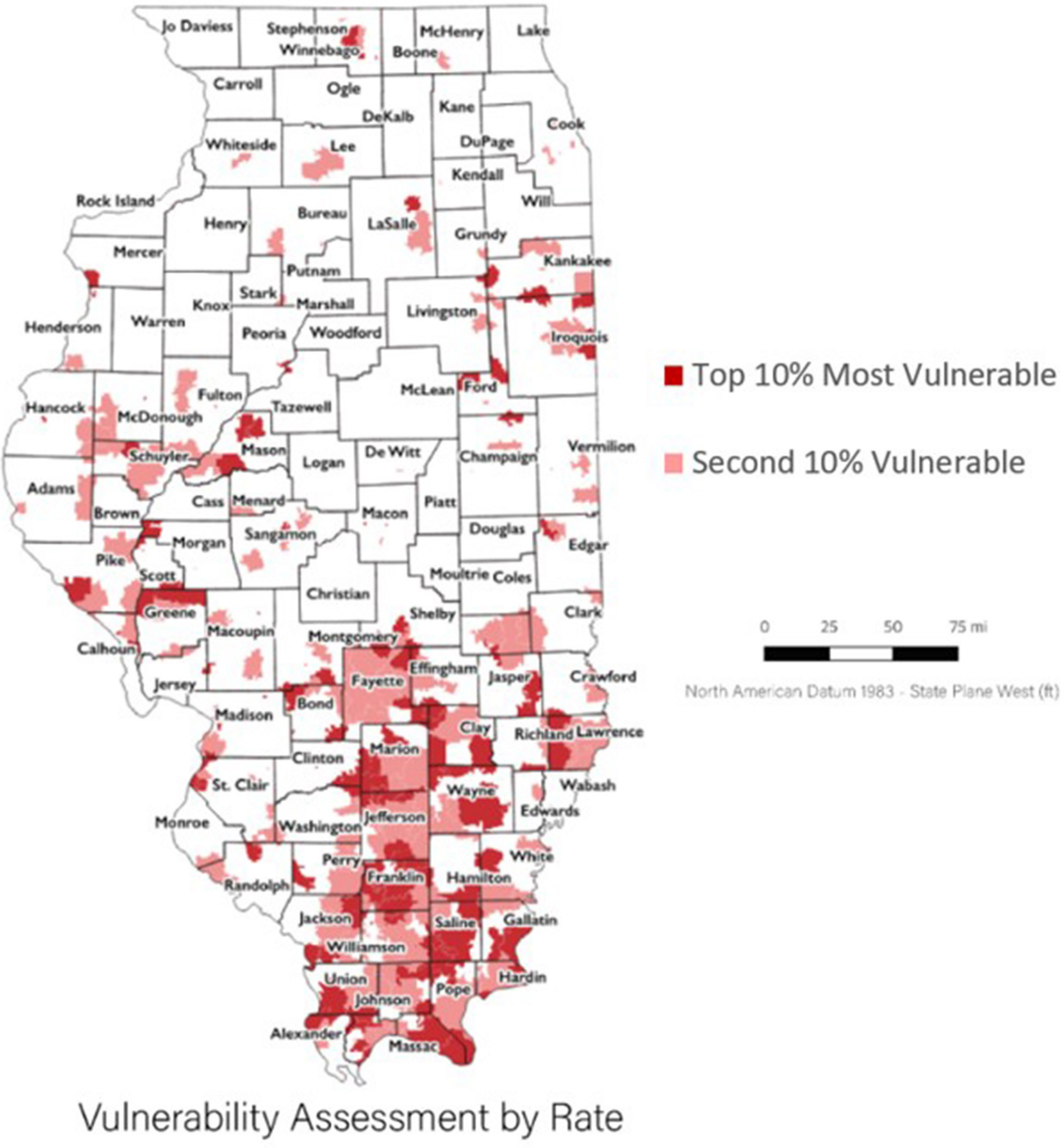

FIGURE 1 | Illinois vulnerability assessment by rate.

aspects of the physical environment may impact disease vulnerability. These factors were not included in the nationwide CDC analysis, and were not significant in the county level analysis performed in Tennessee. Of note, in the South Dakota vulnerability analysis, the percent of mobile homes was associated with lower HCV infection rate in minority dominant counties, whereas in white dominant counties, this association was not significant. Given the known relationship between housing and health, this protective effect of race would be important to explore. In studies adjusted by race, homelessness and unstable housing has been shown to be associated with sharing used syringes among people who inject drugs, and higher physical health and mental health morbidity and mortality overall (Maness and Khan, 2014; Auerswald et al., 2016; Rezaei et al., 2020). Unstable housing for renting families can result in poorer health outcomes for caregivers and their children, including increased adult depression and childhood hospitalizations, and in one study the percent of mobile homes has been inversely associated with life expectancy at the census tract level (Sandel et al., 2018; Melix et al., 2020).

The findings above reveal a greater complexity underlying the interplay between demographic, socioeconomic and environmental characteristics that impact HCV risk. In our previous work focused on a predominantly rural southern areas of the state, complex heterogeneities emerged as smaller spatial units were examined and aggregated based on common environmental typologies. In short, rural areas are not monolithic, and the ability to assess risk at the ZIP code level affords jurisdictions, the capacity to finely target relatively high-risk regions regardless of county lines and of state rankings overall.

Additionally, broadening geospatial focus beyond areas of prevalent risk to those of increased vulnerability allows for more diffuse provision of preventive public health activities. State and local health departments may engage stakeholders such as community-based organizations, first responders and other health providers, to review high-risk ZIP codes that may or may not have been areas of concern based on previous service provision. Resources may be directed accordingly to build capacity and/or engage in field activities, such as disease screening as well as harm reduction services including sterile syringe provision, sexual risk reduction, and overdose education and naloxone distribution. The attention to prevention activities on vulnerable and potentially overlooked areas provides an important opportunity to expand investigation beyond active outbreaks as detected through traditional public health data, such as passive HCV and HIV surveillance, syndromic surveillance and overdose surveillance using emergency medical services and law enforcement sources.

Our analysis has several limitations. Associations between the variables and HIV/HCV vulnerability should not be considered causal. HCV infection is known to be under reported, although it is unclear how this may vary across demographic and risk-related variables (Klevens et al., 2014). We did not have access to opioid prescribing data at the time of this analysis. Variables including opioid analgesic dosing and prescriptions per person were significant in the prior vulnerability analyses (Van Handel et al., 2016; Rickles et al., 2018; Wesner et al., 2020). Fatal overdoses in Illinois have been shown to be heterogeneous in type of opioid (prescription vs. illicit) involved, history of antecedent opioid prescribing and race (Abbasi et al., 2020). In prior analyses of the Illinois Prescription Drug Monitoring Program, rural counties in southern areas had disproportionately higher opioid prescription rates, supporting our findings of vulnerability in these ZIP codes[12]. Future analysis including this data would help elucidate the impact of opioid prescribing on HCV risk. Finally, we did not have access to HCV nor HIV treatment data. These data are incompletely available in public health surveillance datasets and are resource intensive to collect (Ly et al., 2015). Given the history of highly restrictive prior authorization criteria for direct acting antiviral medications used for HCV required by the Illinois Medicaid program, and the well-accepted strategy of treatment as prevention for HIV, incorporating this information into future models could present a more complete assessment of risk (Dieffenbach and Fauci, 2009; Granich et al., 2009; Montaner, 2011; Barua et al., 2015). Identifying vulnerable ZIP codes through our analytical approach may allow local jurisdictions to focus their limited resources on collecting treatment data at a hyper local level.

Our study updates prior, US-wide county level analysis of geospatial risk for HCV and HIV outbreak related to injection drug use with a fine-scale approach. We validated and extended previous findings to identify additional areas of vulnerability. Priority recommendations defined by the state as a result of the analysis include increasing access to harm reduction services, specifically sterile syringe services, naloxone access, infectious disease screening and increased linkage to care for HCV and opioid use disorder[13]. ZIP code level rankings allow local public health jurisdictions to more finely tune surveillance and preventive measures and target activities at a sub-county level.

DATA AVAILABILITY STATEMENT

The data analyzed in this study is subject to the following licenses/restrictions: confidential infectious disease reporting data. Requests to access these datasets should be directed to Cara Jane Bergo, cara.bergo@illinois.gov.

AUTHOR CONTRIBUTIONS

MP and MK helped form this paper and the overall project. SH and JE helped allow data access and explore ways to implementation, also were consistent editors of the paper. CB worked on the analyses of this paper. All authors contributed to the article and approved the submitted version.

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[12] Opioid Prescribing in Ilinois: Examining Prescription Drug Monitoring Program Data. (2018). Available online at: https://jrsa.org/pubs/sac-digest/vol-28/il-opioidprescribing.pdf

[13] IDPH JVA Report.

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COMMUNITY CASE STUDY
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Community Case Study of Naloxone Distribution by Hospital-Based Harm Reduction Program for People Who Use Drugs in New York City

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Background: In 2017, The Respectful and Equitable Access to Comprehensive Healthcare (REACH) Program at Mount Sinai Hospital became a registered Opioid Overdose Prevention Program (OOPP) and received funding from the New York City Department of Health and Mental Hygiene to develop a program to provide overdose education and naloxone distribution (OEND) training to at risk population and bystanders. We report on the programmatic quality improvement initiatives conducted.

Methods: From April 2017 to December 2020, the REACH OOPP conducted 290 opioid overdose reversal trainings, throughout the Mount Sinai Health System and in multiple other community settings. OEND training was at times offered alone and in other settings alongside Hepatitis C Virus point of care testing. Additionally, a "train the trainer" model was implemented whereby medical students and nurses at outpatient clinics were trained to train others.

Results: There were 4235 naloxone kits distributed to 3,906 participants. The training venues included hospital settings (patients and medical staff), public events, substance use programs, educational facilities, homeless prevention programs, faith-based organizations, alternative to incarceration programs, and community-based organizations. We implemented two types of training. During outreach sessions, we utilized one-on-one personalized sessions to train bystanders. When training clinic staff in the "train the trainer" model we utilized a standardized didactic presentation with slides. The two top reasons participants reported for being trained were "Just in case I see someone overdose" (59.3%) and "I'm worried that someone I know will overdose OR that I will overdose" (20.2%).

Conclusion: The REACH program at Mount Sinai Hospital developed an effective model to train community bystanders and health care staff by leveraging administrative support and building on broader programmatic initiatives to promote drug user health and stigma-free care for people who use drugs. Hospitals do not currently mandate staff training or keeping naloxone stocked at inpatient units or outpatients clinics posing a challenge when implementing an OEND program in this setting. A recommended policy change needed to

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decrease overdose deaths is for hospitals to be required to implement systematic naloxone education and access for all health care personal and at risk patients.

Keywords: naloxone, narcan, overdose, opioid education, naloxone training, take-home-naloxone, overdose education and naloxone distribution, COVID-19

INTRODUCTION

Unintentional drug overdose deaths related to opioids have been on the rise in the United States (U.S.) since 1999, becoming a public health concern that has affected a wide spectrum of Americans. The rate of drug overdose deaths involving heroin, a "natural" opioid derived from opium, increased by 18% per year from 2014 to 2016 (Hedegaard et al., 2017). Deaths involving synthetic opioids other than methadone, including fentanyl, a synthetic opioid 30 to 50 times stronger than heroin, increased by 88% per year from 2013 to 2016 (Hedegaard et al., 2017). The total cost of the opioid overdose epidemic in the U.S., including costs associated with the use and misuse of prescription and illicit opioids in 2015, has been estimated at over $500 billion (Haegerich et al., 2019; Council of Economic Advisers, 2020). Interventions that stem the mortality and cost related to opioid overdose are a major public health priority.

Naloxone is a competitive opioid antagonist that temporarily displaces opioids in the brain and reverses opioid-induced respiratory depression (Doyon et al., 2014). Naloxone is a safe, rapid, effective and easy-to-use (nasally administered) medication, without any psychoactive effects and no potential for abuse (Bazazi et al., 2010). The increased opioid overdoses have shifted naloxone from emergency rooms to first responders such as police, emergency medical technicians, and the friends and family of overdose victims (Skolnick 2018). Naloxone has played an essential role in community-based health promotion programs, proving an invaluable tool for laypersons who witness an overdose. Research has demonstrated that naloxone distribution to laypersons provided by community organizations may decrease opioid-related deaths in those communities (Wheeler et al., 2015; Opioid Overdose Prevention Programs Providing Naloxone to Laypersons — United States, 2014, 2020).

The U.S. Department of Health and Human Services (HHS) launched a comprehensive campaign called the "5-Point Strategy" to better combat the opioid crisis and naloxone distribution was one of key components (Division, 2018). In April 2018, the U.S. Surgeon General issued a public health advisory on naloxone and opioid overdose encouraging health care providers to play an active role in naloxone awareness, availability and administration (Sohn et al., 2019). In 2016, Public Health Law Section 3309 10 NYCRR 80.138 in New York authorized clinical directors (physicians, physician assistants or nurse practitioners) to prescribe naloxone to train overdose responders and anyone likely to experience or witness an overdose. In New York City, naloxone can also be directly dispensed by pharmacies without a prescription and with or without patient insurance.

Overdose Education and Naloxone Distribution (OEND) programs have therefore emerged in multiple settings as a resource for people at risk of witnessing or experiencing an overdose. In this paper, we describe how our primary-care-based program, The Respectful and Equitable Access to Comprehensive Healthcare (REACH) Program at Mount Sinai Hospital in New York City, developed an OEND model to address the opioid epidemic in our community inclusive of the general public [not only targeting people who use drugs (PWUD)], and the broader impact of this initiative in the larger hospital system. Our harm reduction-oriented approach involved interventions targeting stakeholders at many levels in our healthcare environment and fostering new partnerships. OEND sessions provided an opportunity to destigmatize PWUD and equip the public with a tool to potentially prevent an opioid overdose death. In this paper, we describe our OEND programs and address the multitude of challenges and lessons learned from our experiences as an OEND program. The authors of this paper implemented the community case study described.

BACKGROUND AND RATIONALE

Literature on the impact of take-home naloxone on PWUD first emerged in the late 1990s. OEND was created as a harm reduction tool by PWUD and advocacy agencies to empower PWUD and their communities. (Dettmer et al., 2001; Maxwell et al., 2006; Winhusen et al., 2017). Syringe Service Programs (SSP) are ideal places for OEND because they provide culturally relevant services designed to reach persons at high risk for experiencing or observing an opioid overdose (Lambdin et al., 2020). However, naloxone should be available in multiple settings to ensure equitable access to OEND to all individuals, including those that do not access harm reduction services through SSPs. Recent articles have focused on pharmacies and health systems as viable sources for broader naloxone distribution to bystanders and substance users in rural and urban areas (Drainoni et al., 2016; Akers, Hansen, and Oftebro, 2017; Devries, Rafie, and Polston, 2017; Morton et al., 2017). A pilot study developed a four-step program for OEND at The Veterans Health Administration (VHA) that focused on identifying target populations, garnering support, training staff members, and implementation (Peckham and Boggs, 2016). Inpatient medical OEND integration was explored in another pilot study that enrolled newly admitted patients who had used opioids in the year before admission, exposed them to a short training video, and gave them a take-home naloxone supply (Jakubowski et al., 2019).

Several barriers to OEND in clinical settings were identified in these and other studies For example, Peckham et al. found that when implementing the OEND pilot program at VHA, providers felt that only mental health or substance use providers should distribute take-home naloxone due to familiarity with substance use disorders. Providers raised concerns of a possible increase in opioid consumption given the availability of the reversal agent. Informing providers of previous programs' successes in reducing opioid use was key for implementation (Peckham et al., 2016). Another study attempted a broader evaluation of opioid overdose prevention initiatives, by surveying 18 naloxone training programs in Ohio and identifying barriers to widespread medical distribution. The authors found that stigma surrounding opioid use and the cost to purchase and dispense naloxone were preventing optimal implementation (Winstanley et al., 2016). The pilot study examining OEND among hospital inpatients also described limited hospitalization times as a barrier to effectively training all inpatients. Furthermore, they proposed expanding the classification of opioid-related events as a universal assessment rather than targeting only those admitted with opioid-related diagnoses to broaden the eligible pool of participants (Jakubowski et al., 2019).

The REACH Program at Mount Sinai Hospital is located in East Harlem, an area of New York City with a high prevalence of opioid overdose deaths. REACH staff implemented OEND during community outreach events and in some settings OEND was accompanying by hepatitis C virus (HCV) testing. REACH also pioneered multiple initiatives that impacted other hospital areas, including creating a curriculum for medical students and residents, providing a once-a-month naloxone training outside of the main hospital cafeteria, and working together with the emergency services department to identify patients with a substance use disorder for overdose education and naloxone distribution. Our findings are based on almost four years of experience (2017–2020). We outline REACH's naloxone program structure while detailing the successes and difficulties of OEND in three settings: 1) community outreach, 2) primary care clinic, and 3) hospital setting.

METHODS

Setting

The REACH program is a community-based program at the Mount Sinai Hospital, a large urban academic medical center. The REACH Program receives funding from the New York City Department of Health and Mental Hygiene. n.d. "Naloxone", 2020 (NYC DOHMH) and New York State Department of Health (NYS DOH). In April 2017, the REACH Program became a legally registered Opioid Overdose Prevention Program (OOPP) funded by the NYC DOHMH to provide overdose education and naloxone training.

The REACH Program has two main components: 1) an outpatient primary care clinic for persons with HCV infection and/or substance use disorders, and 2) community outreach. The program is located in an epicenter of unintentional drug overdoses in NYC. East Harlem experienced 56.1 deaths per 100,000 residents in 2018 compared to 20.5 per 100,000 residents in the same year in NYC (NYC DOHMH, 2019). The outreach team at REACH began by providing OEND in East Harlem and expanded training programs over time to other boroughs (Bronx, Queens, and Brooklyn) in need of overdose prevention training. Efforts to recruit interested participants started during outreach events at health-fairs, substance use programs, homeless shelters, faith-based organizations, and re-entry programs. Community-based point of care HCV testing was a major ongoing focus of the program, and OEND was offered alongside this service. Naloxone kits were provided to participants for free once training was completed.

The REACH OEND efforts in the outpatient setting led to a domino effect providing the opportunity to impact multiple areas in our health system. This effort began with our model of "training the trainers" which allowed the program to expand naloxone distribution by increasing the number of individuals able to train others. The training follows two different formats depending on the target audience: 1) For clinical staff, we utilized the "train-the-trainer" model, with the purpose of educating attendees on how to train other staff and patients on OEND, 2) For bystanders during outreach sessions, we provided shorter and more personalized training (one-on-one).

Program Description-Opioid Overdose Prevention Training

Our program provided overdose education and distribution of intranasal naloxone (Narcan®) rescue kits to self-identified or interested individuals likely to experience or witness an overdose. The training was performed by five certified patient navigators and one peer outreach worker from REACH based on the NYC DOHMH "Save a life. Carry naloxone" training. The training objectives were 1) to increase the number of people able to train others to distribute naloxone ("Train-the-trainer" sessions), 2) train the community to become opioid overdose responders, 3) present naloxone as a harm reduction tool 4) promote REACH services including primary care for PWUD, HCV testing and treatment, and office-based buprenorphine treatment and, 5) education on how to refer a patient by phone or email to REACH.

Naloxone rescue kits included a patient handout with instructional information in English/Spanish, two non-latex gloves, one rescue breathing mask, a certificate of completed training, information to call REACH for naloxone refills, and two naloxone (Narcan®) single-use intranasal spray (0.4 ml in each nostril for a total of 0.8 ml). Participants were instructed to administer one dose and wait 1–2 min. A second dose was included if the first dose failed to reverse overdose symptoms. At the end of each training, participants were asked to complete information regarding demographics (gender, race/ethnicity, zip code of the residence), how they planned to use the naloxone rescue kit and, if they had received a kit before.

Naloxone rescue kits were given to participants without an individual prescription under a standing order, allowing for distribution without a physician present and without any cost.

The curriculum for the trainings included education and techniques in overdose prevention and management including: 1) definition of an opioid, 2) fentanyl's presence in other drugs, 3) reducing overdose risk, 4) naloxone as a harm reduction tool, 5) assessing for an opioid overdose, 6) seeking help by calling 911, 7) delivering intranasal naloxone, 8) information on aftercare including potential withdrawal symptoms (recue position), 9) information about the Good Samaritan Law, and 10) brief education about REACH Program services.

Types of Trainings

Train-the-Trainer Model

Trainings directed to clinical staff including medical students, medical residents, nursing staff, and other health care staff. REACH utilized an hour long PowerPoint presentation (see **Supplementary Presentation S1**) based on "Save a life. Carry naloxone" (Naloxone–NYC Well (cityofnewyork.us). The trainings addressed preventing, recognizing, and reversing opioid overdose, an overview of the most current data about unintentional drug deaths in New York State, and basic information about REACH services. Sessions emphasized naloxone as a harm reduction tool, and participants learned how naloxone could be a point of engagement for PWUD to discuss their drug use and potential treatment modalities. After the session, attendees were encouraged to train others utilizing the "Train-the-trainer" model. The intent of this approach was to expand OEND throughout the hospital. Sessions were led by a physician or patient navigator with a background in health sciences.

Training requests were at times for one-off sessions and at other times for a more integrated multicomponent collaboration between the REACH program and various hospital divisions.

A1) Medical Students and Residents

Medical students at the Icahn School of Medicine at Mount Sinai have a harm reduction interest group. This group approached REACH as a coalition partner, and together medical students and REACH staff created a harm reduction educational power point presentation accessible to all first-year medical students. This presentation was subsequently included as part of medial students' orientation, and served as a recruitment tool for new coalition participants. Additionally, the OOPP's Medical Director created a 30 min presentation for internal medicine resident physicians. The presentations followed the "train-the-trainer model" with the intention of continued training of incoming first-year medical students by residents.

A2) Nursing Staff at Outpatient Clinics

REACH also provided training for outpatient nursing staff in a variety of primary care and specialty settings (e.g., pain management). Providers that identified a patient at risk of overdose or a family member of someone at risk were instructed to refer patients to trained nurses in these settings who then provided OEND to participants. The REACH program stocked nursing stations in these outpatient clinics with take-home-naloxone for distribution.

A3) Other Healthcare Staff

REACH provided OEND to healthcare professionals from various specialties familiar and unfamiliar with substance use disorders. The training encouraged the providers to call the REACH program at the time of conducting OEND to determine the appropriateness of a referral and, if with an at risk-patient, to arrange a "warm handoff' to a REACH staff member (patient navigator or peer outreach worker). If the patient was interested, an appointment to the program was offered and scheduled at that time.

Training the Community

One-on-One Trainings

The bulk of these efforts by the REACH outreach team (patient navigators and peer outreach worker), was in providing OEND trainings in settings outside the hospital, such as public events, substance use treatment facilities, or re-entry programs. The goal was to reach the community in diverse settings to capture at-risk populations and educate a wide range of community members. This type of training covered the nine points mentioned in the curriculum in a more summarized manner, highlighting key elements; assessing for an opioid overdose, seeking help by calling 911, delivering intranasal naloxone, information on aftercare including potential withdrawal symptoms (recue position), and information about the Good Samaritan Law. The trainings were designed to assess and build on potential overdose bystander knowledge in a 10–15 min one-on-one talk with any interested attendees.

Because the OEND was met with immediate interest in the community we increased the number of outreach sessions and broadened our presence. As one example, we created partnerships with churches in high-risk neighborhoods. Participation during outreach sessions offered an opportunity to further educate the community about REACH services. By word-of-mouth, participants referred peers for training.

Monthly quality improvement meetings were held with the medical director, program director, project coordinator, and relevant staff to discuss progress on the project, new initiatives, improve quality, and review data. The data collection informed the meetings, shaped the program's next steps, and provided a monthly space to reflect on lessons learned. REACH team also attended a yearly meeting with the funder and submitted monthly and quarterly reports that provided additional opportunity to reflect on and synthesize lessons learned in the project.

Opioid Overdose Prevention Programmatic Adaptation During COVID-19

During the COVID-19 pandemic, many OOPPs had to modify their services of overdose education and naloxone distribution. In an effort to fill this gap and support increased access to free naloxone during the pandemic, the NYC Department of Health and Mental Hygiene (NYC DOHMH) launched the NYC Emergency Overdose Rescue Kit Pharmacy Pilot in June 2020. The pilot was established by a collaboration between the NYC DOHMH and two chain pharmacies in the 15 neighborhoods with the highest rates and numbers of overdose mortality.

Pharmacies participating in this pilot (n = 15) dispensed free overdose rescue kits to any individual who requested one. Kits are accessible without an ID or insurance coverage. NYC DOHMH posted a list of participating pharmacies on their website.

Given incidental patient reports about difficulty obtaining naloxone from pharmacies, REACH decided to evaluate the NYC Emergency Overdose Rescue Kit Pharmacy Program given its importance as a distribution channel during the COVID-19 pandemic. REACH obtained an IRB exemption to implement a protocol to visit these 15 pharmacies and determine ease of accessibility and barriers to obtaining naloxone. REACH staff visited these pharmacies unannounced and without identifying themselves requesting pharmacists/technicians to dispense naloxone. Information was collected regarding availability, cost, and formulation (intramuscular, nasal spray, etc.).

Data Collection

The REACH OEND Project was reviewed by the Department of Medicine Quality Improvement Committee and it was designated as a Department of Medicine Quality Improvement Project and not human subject's research. The data presented on the REACH OEND program are quality improvement metrics which were routinely collected as part of REACH's clinical operations for the purpose of program evaluation and improvement. We also present findings from the Pharmacy Outreach project related to the larger REACH OEND program.

As a requirement to receive a naloxone kit, each participant filled out a Naloxone Recipient Form (NRF) which included basic demographic questions such as zip code, race and/or ethnicity, age, experience receiving or using naloxone, and the reason to acquire a kit. The form also had a section filled by the session trainer which specified the program and address of the OOPP conducting the training, the number of kits received by the trainee, expiration date of the naloxone, location of the training, and the name of the trainer. The back of the NRF provided a designated space for the participant to write their name, although participants were advised that a signature or initials would be suffice and were given the option to refuse or leave the section blank if desired.

Information collected from the NRF was then used to create a database in Excel format which served as the reference for the information sent to the NYC DOHMH in the Site Summary Sheet each month and the Quarterly Reports submitted through NYCoverdose.org. In addition to the information in the NRF, the database collected the number of trainings per reporting period, type of organization or location where the training was performed, and the overdose reporting forms filled or communicated to the OOPP.

RESULTS

Community-Based Overdose Education and Naloxone Distribution

From April 2017 to December 2020, the REACH Program distributed 4,235 naloxone kits to 3,906 participants at 290 direct trainings and trainings provided by those we trained. The majority of trained participants identified primarily as black (29.4%), Hispanic (24.2%), or white (22%), and the mean age was 42 years (range 14–97 years old). Data collection did not capture demographics related to gender.

Information collected from the NRF indicated that the three top reasons for getting a kit were "Just in case I see someone overdose" (59.3%), "I'm worried that someone I know will overdose OR that I will overdose" (20.2%) and "I work with people who use drugs as part of my job" (18%). There were 275 overdose prevention trainings conducted by REACH in which 3,308 people were trained. Of the 3,308 trained participants, almost all (3,301) agreed to receive one or more kits for a total of 3,724 kits distributed. See **Figure 1** for the setting in which these 3,724 kits were distributed.

Naloxone Distribution by Setting

Hospital Setting

We distributed 40% (see **Figure 1**) of the take-home-naloxone kits within Mount Sinai Hospital. Distribution settings included the hospital's cafeteria, a diverse range of specialty settings within the Mount Sinai Hospital (see **Figure 2**), the waiting rooms of outpatient clinics, the medical student run free clinic for East Harlem residents, the emergency department, nurse stations at outpatient clinics, student harm reduction coalition trainings to first-year medical students, trainings to first-year Mount Sinai residents, REACH support groups and Community Advisory Board meetings. In these settings, we targeted the general public, health care staff, and patients utilizing hospital services. When training medical students, medical residents, and staff from various specialties we utilized a power point presentation. However, we used 10–15 min one on one talks when training bystanders at the hospital cafeteria, waiting rooms, free clinic, emergency rooms, and nurse stations as well as during REACH hosted events.

a) Naloxone Education Outside the Hospital Cafeteria

The hospital cafeteria is located in the main hospital, open to Mount Sinai employees, patients and family members. Our program coordinated a monthly session open to the public (patients clinic and non-clinic staff) during high traffic times, outside the entrance to the hospital cafeteria. The sessions started in August 2019 and a total of 213 kits were distributed among participants over the course of 8 months until the COVID-19 pandemic began. We found that these sessions enabled our team to interact with a wider variety of staff than did our targeted trainings. Additionally, we expanded education about REACH Program services. These trainings increased the number of referrals to REACH (for services including primary care for PWUD and to provide additional OEND trainings).

b) Naloxone by Specialty

REACH was able to train personnel in nine specialty disciplines to distribute 91 naloxone kits (**Figure 2**).

c) Involving Medical Students

Medical students at the Icahn School of Medicine at Mount Sinai quickly became interested in helping to distribute naloxone and educate community members about overdose prevention.

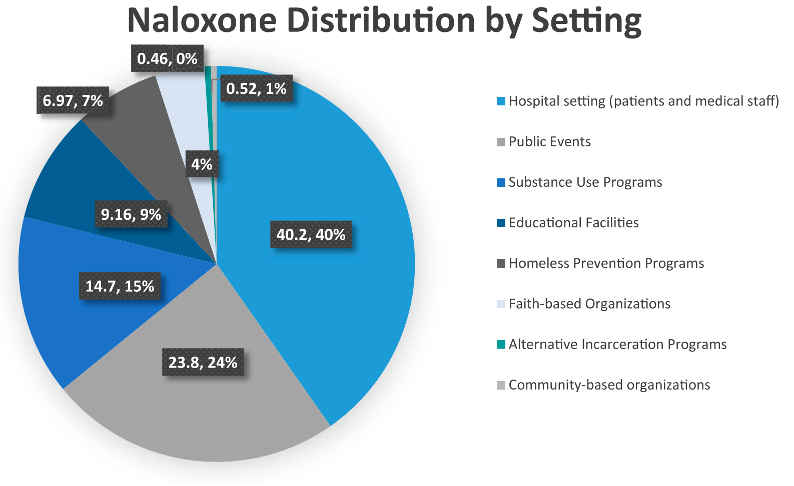

FIGURE 1 | Naloxone distribution by setting.

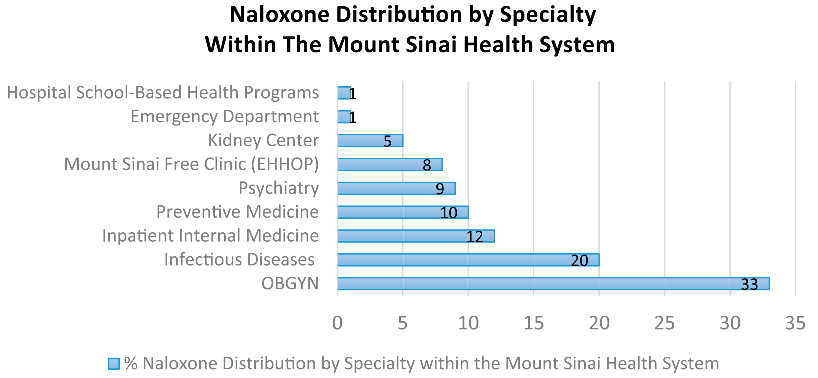

FIGURE 2 | Naloxone distribution by specialty within the Mount Sinai health system.

REACH staff and medical students created a brief curriculum to increase medical student knowledge on substance use and harm reduction principles including doing rotations at syringe exchange programs. All first-year medical students were trained and received naloxone kits during orientation week. Additionally, trained medical students distributed naloxone to at-risk patients during emergency department overdose visits twice a month in the outpatient clinic waiting rooms, and during East Harlem Health Outreach Partnership (EHHOP) sessions. EHHOP is a free clinic at Mount Sinai hospital run by medical students and residents to serve the uninsured. Medical students also volunteered during REACH community outreach sessions.

d) Nurses Provide OEND to Patients

The REACH Program partnered with nurses at the Internal Medicine Associates (IMA) outpatient clinic. REACH is co-located within IMA which offers various primary care and specialty services. REACH provided naloxone training to the nurses via a 45 min Power Point presentation utilizing the train-the-trainer model. Our goal was to identify nurse champions who would in turn identify potential patients at risk, provide OEND and keep an inventory of the kits at each nurses station. However, after the training, only two nurses were interested in becoming champions. Most felt they could not incorporate the role into their daily tasks. We shifted our focus and asked providers (including residents that received the naloxone training by our team) to refer patients at risk or their family members to the nurses. Nurses provided 15 min one-on-one training with patients identified by the clinicians and collected the NRF forms. Our team kept an inventory of the five kits per firm (4 firms participated) and restocked them every two months.

Public Events

This setting represented 24% of our OEND efforts (see **Figure 1**). They included events hosted by the East Harlem community, such as the Juneteenth Health Fair, the Malcolm Shabazz Harlem Market, and a theater performance about substance use. Our team also attended events tailored to at-risk populations, such as one hosted by a re-entry program offering free haircuts. There were events hosted by REACH, such as a Medication Assistance Waiver Training for medical providers and the International Overdose Awareness Day (IOAD) remembrance event. We also participated at health fairs for the Metropolitan Transportation Authority staff.

Additionally, building on our hepatitis C testing collaboration with the Georgian community, we participated in an annual festival celebrated by Georgians. We offered OEND at a supermarket in one of the top five zip codes for rates of unintentional drug poisoning (overdose) (NYC DOH MH 2012-2013). Other public events were hosted by the Mount Sinai hospital or community members. We used a 10–15 min one-on-one talk model at all events. In some settings we offered hepatitis C testing, but in the majority, we only did OEND. At some of the events, we encountered an audience with previous naloxone experience. For example, at the IOAD, participants shared their personal and family experiences with overdose and naloxone administration.

Substance Use Programs

We collaborated with inpatient substance use treatment programs, transitional housing programs including halfway housing, long-term residential, and outpatient substance use treatment programs, and a nursing residential healthcare facility. Based on the program's needs, we provided only OEND, or we offered naloxone along with HCV testing. While offering both services, we had two approaches: 1) during HCV testing, participants completed a brief intake that included risk factors. If a patient had active substance use or was at risk of an opioid overdose, our outreach team offered naloxone via a one-on-one training as the participant waited for the rapid antibody HCV testing results. 2) If we had a larger group, we provided a 15 min oral presentation on naloxone and then offered HCV testing. As in the public events setting, REACH encountered individuals with previous knowledge of naloxone administration, opioid overdose, and in some cases, death due to an overdose.

Educational Facilities

The REACH Program partnered with community health centers at various community colleges in NYC. Our team provided OEND during the community health centers' presentations of services to first-year students. At other colleges, our team distributed naloxone through 15 min one-on-one talks at college health fairs. We trained research coordinators and staff at a university conducting a study on PWUD. Additionally, we trained health staff from an adolescent health center for students at a charter school.

Community-Based Organizations

We collaborated with the Mexican consulate by giving an oral 45 min Power Point presentation in Spanish to participants in the waiting room of the consulate. We partnered with a community center in East Harlem by offering OEND to groups run by agencies co-located in the community center. Furthermore, we hosted several sessions at an LGBTQ center in NYC. In some of these sessions, REACH offered HCV testing and OEND to all participants utilizing the same approach described for the substance use setting.

Homeless Prevention Programs

The REACH Program teamed with agencies that provide temporary and permanent housing with supportive services to homeless individuals at various locations. In some of these sessions, REACH offered HCV testing and OEND to all participants utilizing the same approach described for the substance-use setting. Additionally, we distributed naloxone in the streets by collaborating with a mobile soup kitchen bus agency that traveled to at-risk neighborhoods targeting the homeless population. One of the locations was near one of the largest methadone programs in the country. OEND was provided in 10–15 min one-on-one sessions or in small groups. A bilingual (English/Spanish) REACH member provided culturally and linguistically appropriate training in Latinx neighborhoods. In this setting, we often encounter individuals' already knowledgeable about naloxone administration, opioid overdose, and overdose death. Additionally, individuals in these settings often mentioned two main themes: 1) they were previously trained but did not get a kit after the naloxone training, or 2) owned a kit and wanted an additional one due to the high risk of overdose for themselves or people around them.

Faith-Based Organizations

REACH collaborated with one of the chaplains at the Center for Spirituality and Health at Mount Sinai's Icahn School of Medicine that introduced REACH to various faith-based organizations, including the Salvation Army. OEND was offered at small health fairs for members of the faith organizations or after religious services. OEND was provided by 10–15 min one-on-one sessions.

Alternative to Incarceration Programs

We hosted various group sessions at a re-entry from incarceration for program participants. We also provided a 45 min Power Point presentation to staff at a Brooklyn Courthouse.

Naloxone Distribution During the COVID-19 Pandemic

Pharmacy Outreach Evaluation

During August and September 2020, REACH staff made a single visit to all 15 pharmacies that were part of the NYC DOHMH Emergency Overdose Rescue Kit Pharmacy Pilot. These pharmacies were located in all five boroughs Bronx (5), Brooklyn (3), Manhattan (4), Staten Island (2), and Queens (1). We evaluated 1) the percentage of pharmacies that had naloxone in stock; 2) the types of naloxone available; 3) the reason for not having naloxone in stock; and 4) whether education was provided when the kit was dispensed.

Of the 15 pharmacies, 10 (66.6%) pharmacies dispensed naloxone to our staff. When dispensed, pharmacy staff did not request ID or insurance information. All kits were given without any cost and within a few minutes of speaking with pharmacy staff. All the kits contained two doses of naloxone nasal spray

(Narcan®), two non-latex gloves, a face shield for rescue breathing, and an insert with Spanish/English instructions for responding to an overdose.

At the other five (33.3%) pharmacies, our staff was not able to obtain naloxone. Three pharmacies did not have naloxone in stock when visited. One pharmacy refused to dispense naloxone without a prescription, and one pharmacy was closed on weekends and had limited hours. These results were shared with the NYC DOHMH. In response, NYC DOHMH actively worked with pharmacies to ensure program awareness and adequate naloxone stock. Additionally, NYC DOHM updated the online participating pharmacies list and included the business hours and phone numbers of each pharmacy participating in the pilot.

REACH OEND Program Shift During COVID-19

Our program is located at what was the epicenter of the U.S. COVID-19 pandemic during March-April of 2020. We had to find creative ways to continue to provide naloxone trainings during this time. NYC DOHMH authorized OOPPs to mail naloxone kits to participants in response to the public health emergency. Medical students attempted to contact a total of 509 patients that were identified as at risk for an opioid overdose (patients prescribed buprenorphine or with history of active opioid use). Of those 509, 338 were patients from the REACH program; the remainder were patients in the Emergency Department or Inpatient services that presented with or were at risk of an overdose. The medical students provided training to 90 of these patients, 84 of whom received an overdose kit by mail or through the attending physician/care team at discharge. Six patients who received remote naloxone training did not want a kit mailed for reasons including already having one at home. In addition, we began a monthly Zoom OEND session open to the public. Sessions were promoted using social media (Instagram and Twitter) and through our program newsletter. The sessions were hosted by one of our team members for approximately 15 min utilizing the same principles of our in-person sessions, and naloxone kits were mailed to participants after the sessions. From May to December 2020, we hosted 14 virtual trainings and mailed 276 naloxone kits.

DISCUSSION

Expanding naloxone distribution for treatment of opioid overdose has been a focus of policy at local, state and national levels in the U.S. Our program illustrates several methods by which naloxone distribution can be facilitated.

Lessons Learned

Lessons Learned From Training Bystanders

Hepatitis C Virus Testing and Naloxone Distribution

Before becoming part of the OOPP, our community outreach was focused solely on HCV testing and education; adding naloxone distribution/overdose education to our services provided an opportunity to partner with a broader range of organizations. This addition increased our collaboration with other programs such as homeless shelters, and court-mandated residential and chemical dependency treatment programs and, in turn, allowed us to engage a patient population that is often distrustful of the healthcare system and build more meaningful relationships with the community.

While hosting training events, many participants disclosed the need for additional services such as stigma-free risk reduction counseling, office-based buprenorphine treatment, HCV testing or treatment, overdose response training, mental health services that offer support groups. Naloxone distribution provided an entry point into care, and our team was able to either provide information about services to participants and family members or schedule an appointment for requested services on the spot.

Reaching Participants With Limited Literacy and/or English Proficiency

Naloxone education poses various challenges depending on the setting and population. Many program participants had limited literacy and/or English proficiency. To overcome these challenges, we aimed to have a bilingual staff member in locations where we knew we would encounter a large Spanish speaking population and both the training literature and data collection forms were printed in Spanish. In the case of the Georgian community, we solicited volunteers who could provide cultural context and translation into Georgian and Russian (including translation of the NRF forms).

Lessons Learned From Training Clinical Staff

REACH Interfacing With the Larger Health Care System

REACH's monthly hospital cafeteria trainings made clear to us the tremendous overlap across health care professionals, other hospital staff, community members, and patients. Often those trained at these events were members of two or more of these groups. Many of these trainings were done with a diverse group of attendees, including the general public, health staff, PWUD, and family members of people at-risk for an opioid overdose. We found that holding public OEND with a heterogeneous group membership had the potential to decrease institutional stigma associated with drug overdose. Based on comments received from trainees and new referrals from new departments to provide trainings; we believe that these in-house trainings contributed to shifting the culture within Mount Sinai Hospital around the care for opioid use disorder and promoted a more humane treatment of survivors of opioid overdose.

The REACH Program OOPP initiated actions within the larger health system to address opioid overdose risk. Naloxone kits were made available at nurses' stations in the primary care outpatient clinics and providers and nurses were able to give naloxone kits to at-risk patients. More could and should be done. For example, if a patient is prescribed an opioid, the electronic health system could trigger a reflex order for naloxone to the patient's preferred pharmacy. As another example, the Mount Sinai emergency department started a collaboration in early 2020 that connects participants who have had a near fatal overdose to peer "wellness advocates" who are deployed to the ED to offer overdose education, (Welch et al., 2019), naloxone, linkage to care (including to the REACH Program) and supportive follow-up up for 90 days.

Medical Students and Residents Role in OEND

As part of an academic medical center, we expanded naloxone distribution to first-year medical students and resident physicians who, after being trained, were able to train others. The residents in turn increased referrals to REACH and to nurses able to provide naloxone training to identified patients.

Empowering Others to Expand Their Naloxone Knowledge (Train the Trainer)

This approached helped broaden our reach by training clinic and non-clinic staff on how to teach OEND to others. By empowering other hospital staff (medical students, residents and nurses) we increased sensitivity to conducting substance use assessments, and potentially decreased stigmatization of PWUD.

Collaboration With Other Medical Specialties

Sometimes OEND training was provided as a one-off event, and other times, as part of a multicomponent approach to address substance use in different hospital areas in. We noticed an increased interest in naloxone trainings in the second scenario. For example, when OEND was combined with training on buprenorphine treatment to specialty areas serving patients with a high prevalence of substance use disorders. Naloxone functioned as a tool for teams to collaborate on addressing patients' substance use journeys.

Lessons Learned as a Program

Naloxone Distribution by Setting

Overall, we realized that we succeeded in getting more participants interested in naloxone in some settings as compared to others. Based on audience engagement and trainers' experience, we realized that settings like the hospital, substance use programs, and homeless prevention programs presented an audience very open to learning about naloxone. We noticed that at the substance use programs, some public events that target PWUD or staff working with PWUD, and at homeless prevention programs, most participants (including staff) knew about naloxone administration, overdose survival, and/or had experienced grief from losing a loved one to an overdose. As a natural progression during the presentation, participants and staff shared their own experiences. These moments allowed for clarification of misbeliefs and reinforced the need for adequate naloxone administration. If the training was done as a 10–15 one-on-one talk, REACH staff connected the participants with resources offered by REACH including appointments with one of our providers, and invitations to join the weekly harm reduction group or the Community Reinforcement Approach to Family Training (CRAFT) program.

On the other hand, at events where the public was diverse in naloxone knowledge, our team more often experienced less audience engagement, more stigmatized understandings of substance use, and a lacking of understanding of the purpose of naloxone. In the future, broadening future outreach to the public may help decrease stigma surrounding drug use and expand the use of naloxone.

Lessons Learned During COVID-19

During the COVID-19 Pandemic

We recommend that OEND through Zoom training followed by mailing naloxone should continue post-COVID. PWUD face many barriers to care, and offering multiple options on how to engage in medical care should be best practice.

Pharmacies Naloxone Dispensing During COVID

More than 2,600 pharmacies throughout New York State have naloxone available without a prescription through a standing order (New York State Department of Health n. d.). Although dispensing naloxone through a standing order may seem like an advantage, there's no widespread public knowledge of this option. Both "train-the-trainer" and bystander trainings provided by our program, aimed to address this knowledge gap.

While the NYC DOHMH provides funding and guidelines on how to obtain and replenish inventory of naloxone kits and collects and reports kit distribution metrics, its distribution and event protocol guidance is limited. Consequently, protocols on how to organize events and distribution are left to each OOPP. The New York State Department of Health does provide opioid-related data to support prevention efforts, including timely overdose reporting, which helps identify struggling communities. The NYC DOHMH web site provides information on upcoming training, community-based programs that can be contacted for free naloxone, and access to additional information about naloxone. The website also includes the ability to download the Stop OD NYC app, which provides guidelines to recognize and prevent opioid overdoses while indicating sources of naloxone close to the user (New York City Department of Health n. d.). Nonetheless, additional centralized guidance regarding naloxone distribution could be a useful tool for OEND programs.

Program Challenges

Reporting Naloxone Used

At all training sessions, we encouraged participants to contact the REACH program or NYC DOHMH if they utilized one or both naloxone doses. Many REACH patients have recounted to their medical providers the experiences of using naloxone to save the lives of others or having their own lives saved by someone else using naloxone on them. Reporting the use of the kit to the OOPP from which it was obtained is not a priority at these moments. This presents a challenge to establish a metric of success through reversal reports, and has been a roadblock that other naloxone-based studies have frequently experienced (Enteen et al., 2010; Lewis et al., 2016; Lott and Rhodes, 2016; Bennett et al., 2011; Bennett et al., 2018; Siegler et al., 2017).

Although outcome metrics are limited for naloxone distribution, the ability to provide education on opioid overdose prevention to an at-risk population has merit in itself. While it is difficult to quantify the specific impact of naloxone distribution efforts, the NYC DOHMH announced in August 2019 that there was a decrease in the number and rate of overdose deaths from 2017 to 2018 after seven consecutive years of increasing drug overdose deaths (New York City Department of Health and Mental Hygiene, 2019). Emerging data shows that this positive trend has been dramatically reversed by the COVID-19 pandemic (New York State Department of Health and Mental Hygiene, 2021), making efforts to mitigate overdose deaths even more crucial than ever before.

Lack of Hospital Policies for Naloxone Distribution

Hospitals do not mandate staff OEND training or keeping naloxone stocked at inpatient units or outpatients clinics. Our program faced barriers when trying to train staff and establish protocols for naloxone education and distribution. For example, nurses did not always feel that distributing OEND was in their scope of work. We recommend that hospitals and health care facilities have clear guidelines for training all staff and educating at-risk patients and the general public. Without clear guidelines and policy recommendations, substance use and PWUD will remain stigmatized. The lack of a mandate also limits expansion of naloxone training to other agencies with clinical and non-clinical personnel. If we want to decrease overdose deaths, we need to implement naloxone education and access for all health care personnel and at risk patients and provide the funding to implement this.

Program Limitations

There are limitations to the work presented. The development of the OEND program occurred organically over time in coordination with the evolution of other REACH program initiatives; it was not guided by an a priori systematic framework or logic model. The work was conducted in an academic medical center setting with significant resources and may not be generalizable to other sites with fewer resources. Additionally, REACH benefited from strong institutional and administrative support for its initiatives to enhance services provided to people who use drugs and reduce associated stigma.

Program Recommendations

- Provide OEND alongside other services that are of interest to PWUD
- OEND trainings should be developed for populations with limited literacy and/or English proficiency
- Training non-clinical health care personnel by utilizing the ‘train the trainer’ method can expand the reach of OEND
- Naloxone distribution presents an entry point to expand program collaboration
- Pharmacies can play an important role in OEND
- Holding public OEND trainings with heterogeneous group membership has the potential to decrease the stigma associated with drug overdose.
- OEND guidelines should be established for all hospitals and health care facilities. All health staff should carry naloxone.

CONCLUSION

The opioid epidemic in the United States requires urgent attention. While national policies in the last few years have begun to encourage naloxone distribution as a safe medication to combat opioid overdose fatalities, these measures must result in clear guidelines for health care institutions across the United States in order to be effective in reaching the most vulnerable communities. The REACH program at Mount Sinai Hospital represents a comprehensive model to train bystanders and medical providers to use naloxone while distributing the medication through connections with community partners and hospital staff. REACH’s community-based, harm-reduction approach to overdose prevention and primary care has allowed for outreach through programs previously not linked to Mount Sinai Hospital. While these connections have facilitated increased naloxone distribution in communities across NYC, they would be greatly enhanced if integrated into a systematic and coordinated health system response to the treatment for patients at risk of overdose. Although quantifiable data on overdose reversals with naloxone has been difficult to obtain because of low reporting rates, the successes and roadblocks encountered during REACH’s almost four years of experience as an OOPP can meaningfully shape future policy initiatives In NYC and across the nation. In the process, community-based outreach programs can continue to play an integral role in fighting the opioid epidemic and furthering the agenda to create a more coordinated multi-component response.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusion of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsoc.2021.619683/full#supplementary-material

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Integrating Cognitive Dysfunction Accommodation Strategies Into Behavioral Interventions for Persons on Medication for Opioid Use Disorder

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Background: Cognitive dysfunction is disproportionately prevalent among persons with opioid use disorder (OUD). Specific domains of cognitive dysfunction (attention, executive functioning, memory, and information processing) may significantly impede treatment outcomes among patients on medication for OUD (MOUD). This limits patient's ability to learn, retain, and apply information conveyed in behavioral intervention sessions. Evidence-based accommodation strategies have been integrated into behavioral interventions for other patient populations with similar cognitive profiles as persons with OUD; however, the feasibility and efficacy of these strategies have not yet been tested among patients on MOUD in a drug treatment setting.

Methods: We conducted a series of focus groups with 25 key informants (10 drug treatment providers and 15 patients on MOUD) in a drug treatment program in New Haven, CT. Using an inductive approach, we examined how cognitive dysfunction impedes participant's ability to retain, recall, and utilize HIV prevention information in the context of drug treatment.

Results: Two main themes capture the overall responses of the key informants: (1) cognitive dysfunction issues and (2) accommodation strategy suggestions. Subthemes of accommodation strategies involved suggestions about particular evidence-based strategies that should be integrated into behavioral interventions for persons on MOUD. Specific accommodation strategies included: use of a written agenda, mindfulness meditation, multi-modal presentation of information, hands-on demonstrations, and a formal closure/summary of sessions.

Conclusions: Accommodation strategies to compensate for cognitive dysfunction were endorsed by both treatment providers and patients on MOUD. These accommodation strategies have the potential to enhance the efficacy of behavioral interventions to reduce HIV transmission among persons on MOUD as well as addiction severity, and overdose.

Keywords: opioid use disorder (OUD), behavioral interventions, cognitive dysfunction, accommodation strategies, qualitative analysis

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INTRODUCTION

The opioid epidemic is an on-going public health crisis that continues to plague the US, as Opioid Use Disorder (OUD) diagnoses and overdose rates have exponentially increased in the past 10 years (1). The most common evidence-based medical treatment for OUD is medication for opioid use disorder (MOUD). MOUD is a comprehensive treatment strategy, often used in conjunction with behavioral interventions to reduce HIV and overdose risks. Common behavioral approaches include cognitive-behavioral therapy (CBT), motivational interviewing (MI), and contingency management CM; (2–4). Various psychoeducational counseling approaches are also commonly provided in the context of MOUD (5). Such approaches are often used to increase knowledge, motivation, and coping skills related to addiction and health risk reduction (6). By nature, these behavioral approaches often place cognitive demands on OUD patients, many of whom already experience cognitive dysfunction associated with drug use and related factors.

Cognitive dysfunction, commonly manifested as deficits in attention, executive functioning, and memory (7–11), can dramatically impede engagement and retention in drug treatment (12, 13). Researchers have identified cognitive dysfunction subcategories (including information and motivation constructs) that predict weakened HIV risk reduction behavioral skills and engagement in HIV prevention behaviors among persons on MOUD (14). The strategies used in behavioral interventions for OUD treatments may not be ideally tailored to meet the levels/forms of cognitive dysfunction among this population, thus limiting the efficacy of such interventions. Persons on MOUD often exhibit poorer decision-making and longer deliberation times due to cognitive dysfunction (15, 16). Cognitive dysfunction has been identified as a predictor of poor emotional perception among opioid-dependent individuals on MOUD (17). This poor emotional perception impacts patients ability to differentiate between positive and negative feelings of behavior, decreasing the ability to make rational decisions in regard to preventative behaviors (18). It can also adversely impact treatment outcomes (10, 14) such as treatment compliance, willingness to start and stay in treatment, attendance at behavioral intervention sessions, and lack of perspective on the benefits of treatment (19).

Patients with weaknesses in memory, attention, and communication may benefit from modified intervention content delivery and reinforcement (20). Cognitive dysfunction screening tools have been implemented among persons on MOUD, including the NIH Toolbox Cognition Battery (21) and Brief Inventory of Neurocognitive Impairment [BINI;(22)] to inform treatment protocols. However, cognitive dysfunction accommodation strategies tailored to persons on MOUD have not yet been assessed. Compensatory accommodation strategies (e.g., multimodal presentation of information, memory aids/reminders) have been shown to improve treatment outcomes (e.g., medication adherence, motivation) among other patient populations with cognitive dysfunction (23, 24). Most research on cognitive dysfunction accommodation strategies for behavioral interventions has been performed among people with cognitive profiles similar to those identified in persons on MOUD, including people with ADHD or post-TBI (5, 25, 26). There is a gap, however, in research on how such strategies may best be integrated with behavioral interventions in the context of drug treatment settings. Therefore, it is important to understand cognitive dysfunction among persons on MOUD and carefully match tailored accommodation strategies to limit the influence of such dysfunction in order to improve key treatment outcomes (27).

The aim of this study was to gain insight as to which accommodation strategies may be most useful in maximizing treatment outcomes of behavioral interventions for persons on MOUD. The following research question was used to guide data collection and analysis: "How can the experiences of drug treatment providers and people on MOUD inform HIV prevention efforts in a drug treatment setting?"

MATERIALS AND METHODS

Study Design and Sample

The current study was designed as a phenomenological qualitative method design. Focus groups were utilized to help improve the development of HIV prevention programs in the context of a common drug treatment setting. Using a naturalistic approach, focus groups allowed researchers to collect information from a combined local perspective on this particular concept (28). We conducted separate sets of focus groups to gain insight from key informants- both providers and patients on MOUD. One focus group session was with drug treatment providers, and the other focus group session was with patients on MOUD.

The 10 treatment providers were all drug treatment counselors who provide direct care to patients on MOUD at APT Foundation, Inc. The credentials of these counselors include: Licensed Clinical Social Worker (LCSW), Licensed Professional Counselor (LPC), and Certified Drug and Alcohol Counselor (CDAC). All treatment providers facilitate group level behavioral intervention sessions to patients.

The 15 patients on MOUD all attended the APT Foundation, Inc. drug treatment center. The average age of patients was 51 years old and the average daily methadone dose was 83.6 mg. Four patients starting seeking treatment at the APT Foundation, Inc. as early as 2009, while a half of patients started being medicated at the drug treatment center after 2015. A majority of patients reported polysubstance use (93%) and one third of the participants reported having ever overdosed.

Focus groups were guided by an experienced facilitator who has worked with other collaborators to develop pre-determined open-ended questions, based on previous literature and historical outcomes about the content (29). All screening and focus groups were conducted in a private setting. The study protocol was approved by the Institutional Review Board at the University of Connecticut and received board approval from the APT Foundation, Inc.

Data Collection

A convenience sample of participants was recruited via a variety of established methods in this setting to obtain a diverse sample of people on MOUD who are currently in drug treatment via in-clinic flyers, letters of invitation, and word of mouth recruitment. As the largest drug treatment provider in New Haven, with a census of over 4,500 patients, the APT Foundation, Inc. allowed for ample recruitment opportunities. Based on previous focus group research (29–31), including research on HIV prevention (32, 33), we enrolled 10 treatment providers and 15 patients in treatment from the research site. Recruitment occurred in June 2021 and all focus groups were conducted in July 2021.

Participants were reimbursed $25 for their attendance in each focus group. Participants were pre-screened for cognitive dysfunction using the Brief Inventory of Neurocognitive Impairment (22) BINI, and asked to identify their age, self-identified race and/or ethnicity, gender identity, engagement in drug- and sex-related HIV risk, HIV testing history, and past/present engagement in HIV prevention sessions. Individuals initially screened as eligible were invited to attend an in-person screening to confirm eligibility by meeting the following criteria: (a) at least 18 years or older, (b) in drug treatment and reported injection drug use in the past 30 days, (c) reported engagement in drug- and/or sex- related HIV risk behaviors, (d) are HIV negative, and (e) can communicate (read, write and speak) in English.

Data Analysis

Using an inductive approach, in the context of Grounded Theory (34), the researchers analyzed the information using flexible coding (35, 36), to develop a theoretical basis for how cognitive dysfunction may impede participant's ability to retain, recall, and utilize HIV prevention information, in the context of a drug treatment setting. Audio recordings were transcribed and coded using NVivo software (37). Analytic memos and notes documented during focus groups were also used in developing an index of broad codes (38). Furthermore, analytic codes were constructed, based on the discussion points directly from participant's responses during the focus group sessions. During refinement, the researchers documented consistent trends across responses to further describe and apply in the context of other literature and real life applications of program development (39).

Using a bracketing approach, the researchers aimed to detach from preconceived concepts to avoid misinterpreting what the participants were saying about the content and to remain unbiased in the interpretation of their ideas. An audit trail of decisions, explaining the choices made throughout the study were also considered in the data analysis to maximize validity efforts taken by the researchers (40). Peer debriefing was utilized consistently throughout the research processes, and a second coder independently applied codes to the transcripts to enhance interrater reliability. Cohen's kappa coefficient was used to determine interrater reliability; substantial agreement was found between raters ($k = 0.64$). To maximize internal validity, we conducted a second round of focus groups with the same participants who engaged in the first round, as a member checking strategy, to ensure participants agreed with the information and themes we collected from them. This also provided the opportunity for participants to provide additional clarification about information that may have been brought up in their initial focus group session.

RESULTS

Utilizing focus group discussions, we coded two main themes to describe the responses of 25 key informants, including 10 treatment providers and 15 patients on MOUD. These two main themes were cognitive dysfunction and accommodation strategies. Subthemes of accommodation strategies were also identified, specifying which evidence-based cognitive dysfunction accommodation strategies were supported by key informants for integration into behavioral interventions in a drug treatment setting. Definitions and representative quotations are noted in **Table 1**.

Cognitive Dysfunction

Both drug treatment providers and patients on MOUD acknowledged the levels of cognitive dysfunction among the target population of patients on MOUD, and how it directly impacts their ability to stay engaged and recall information presented during group sessions. One provider stated how "memory is terrible, all around, because of the drug use; it does affect their memory, and the significance of the drugs they're using makes a difference on their memory." Patients on MOUD also mentioned their inability to learn new information.

"I started using when I was 26 years old, and I still have the brain of my 26-year-old self. I haven't been able to learn and process new information since."

When discussing patient's ability to remember information and prioritize their recovery, it was noted that "there's also a lot of contingencies; it depends on if their minds are fully working, and different factors." Cognitive dysfunction was also mentioned in reference to a person's point in their recovery and its influence on motivation.

"It's all on a patient-to-patient basis. You cannot pinpoint what will work for everyone but it depends on where they are at in their recovery, so someone that's abstinent will respond differently to a different incentive than someone who is still actively using. But if you can identify the new clients, new in their recovery, everything you give they will take. They're eager like a kid."

The use of worksheets during behavioral sessions was not supported due to cognitive limitations and low literacy levels, as exemplified by one provider: "We have clients that are functionally illiterate, so anything that needs to be filled out, I try to steer clear of those in general. Same with read alouds: they are always optional for me." Similarly, patients also mentioned difficulties with reading and writing.

"I don't like writing because I don't like to have to think. I do have a hard time thinking, even though I've been clean for 6 years, still my mind still struggles to think about certain things, and it's sad, it really is."

TABLE 1 | Emerging themes and subthemes of focus group discussions with drug treatment providers and patients on medication for opioid use disorder (MOUD).

Theme/subtheme	Definition	Representative quotations
Cognitive dysfunction*	Responses by key informants referring to memory loss, impaired literacy (reading and writing), or low levels of education related to years of opioid use. Includes responses by patients on MOUD recalling a low ability to process new information as they compared to their ability prior to drug use.	• → We definitely have people who can't read or write, so I'll help them and do it verbally with them. • → You get people that have memory deficiency or can't focus long enough to retain what you said. • → I mean maybe it comes down to, I mean maybe there are cognitive limitations, I'm sure there are. • → *I have difficulty remembering information.* • → I know some groups with low levels of education, so I condense my group and be mindful of how I can condense it and use some of the proverbs to make it make sense. I can't use this complicated verbiage.
Accommodation strategies*	Responses by key informants providing strategies to compensate for cognitive dysfunction to increase the ability to understand and retain information presented, optimal for a drug treatment setting	**See representative quotations listed in subthemes (i.e., written agenda, catchphrases, multimodal presentation, memory aids, mindfulness mediation, closure)
Written agenda**	Responses mentioning the benefit of using a written agenda to remain on task, guide discussion, and stay on time during sessions.	• → *I would like to see it because a lot of people like us get side tracked and at least we can get the leader of the group to say, ya know, we gotta move on to this. And we know what we covered.* • → Just to keep people engaged and some instances they get bored so keeping them on track is important. It makes them a part of the session the entire time, cause when I am just talking, they lose interest.
Catchphrases**	Responses referring to abbreviated terminology or simplified verbiage to keep patients engaged and improve retention of information.	• → Put it in different contexts and I paraphrase a lot and I use parallels. I tried to give an example like other similar thing, like a catch phrase. That's why I try to give like a popular saying that would equate to what the situation is, using a different scenario to reinforce the information.
Multimodal presentation**	Responses incorporating multiple methods of presenting information including: simplifying language, hands on demonstrations, visual aids and handouts.	• → I will bring in handouts, and it has to be kind of like a directed handout "1,2,3,4,5, something they can follow along with" Easy Verbiage because they just get bored, pictures, colors. • → I think anything you see or actually do, as opposed to just hearing, will help people remember a lot better. • → Sometimes the translations need to be simplified, and use more cultural terms on handouts would really make a difference. • → I think you would have to cut the steps down to like 3 steps, and be the safest way you can do it in the minimum amount of steps and showing them would be the most helpful. • → When the fentanyl came, I would give them a scenario and discuss the history of fentanyl with them with handouts. I would show them the differences in potency with the handout with visuals. • → *I think it's more useful to do it hands on, cause there are something I thought I was doing right, and I wasn't. I'm more of a hands on learner.* • → Some of my handouts are too extensive for them, so I break them down into portions and simplify them. its complex material so I like to have a handout with visuals. • → *For me, I like the videos, I like documentaries to learn, so that's just me.* • → It depends on how long the video or what it's about, cause something too long it's like "when is it gonna be over?" I would say nothing more than 15 min, anything longer than that is just overload and too much, especially if it's something they're not interested in. • → *A handout to debunk the myths.*

(Continued)

TABLE 1 | Continued

Theme/subtheme	Definition	Representative quotations
Memory aids**	Responses mentioning items that serve as reminders for daily tasks, taking medications, attending appointments, and/or behavioral sessions. Included are responses that refer to text message reminder to help patients remember appointments and medications.	• → *Honestly, anytime I can have something to remind me, it's helpful. I prefer weekly reminders though* • → *For me, it would be helpful and since I started the lady asked me if I wanted text reminders, and those are incredibly helpful.* • → *I think it's just so easy nowadays with cell phones. I Don't think people have much of an excuse to miss their dosing or their sessions, cause ya know especially if you're sending out 2 reminders in a day.* • → *I use the calendar function in my phone, like I even use that MyChart for my doctors' appointments.* • → We put it in the SMART program and set holds on their accounts to remind them. To help them get to their appointments, if we are aware of them. I don't know if we could do much more. So, if we have someone who we want to remind them to follow up with a mental health counselor, we can put it into the system and it will light up on the day. • → Text message reminder for appointments that are automated, like a day before and maybe an hour before or something like that. Yeah, some sort of clever system like that. • → *I say "this week, I have this and this and this" I make lists of what I have for the week. Most of it is in my head, but sometimes I write it down.*
Mindfulness meditation**	Responses encouraging and supporting meditation and breathwork as useful tools to decrease stimulation and increase learning.	• → Meditation is actually good, for the ones who like it, it really works. It relaxes you and puts you in a place you don't want to get up. • → So, I think it's all the distractions like if we could somehow clear a space and make this free from other stuff out and that sort of the environment I like to have. This is where you can clear your head. • → I'll just say let's do some cycles of breathing. And the whole group does it and it just makes them grounded and present, and they like it. • → *Ya know, when you have 10 things on your plate, I think it's good to take a breath to remind yourself why you're here.*
Closure**	Responses mentioning the benefit of summarizing the discussion that occurred in the session of the day to reinforce strategies and lessons taught.	• → *Having everyone say what they learned cause in the 1 h / 45 min group it's good to wrap up.* • → *They just like drilled it in and took their time and made sure we knew what we were doing before we left the group.* • → *I think it would be a good idea just to, at the end, reiterate what the point of being here was and it will help you know who was paying attention.* • → *I think it's good to go over, just so you can reinforce again. And different people have different things to talk about too so ya know I think it's good to end with everyone talking.*

Standard font denotes responses from drug treatment providers and counselors. Italicized font denotes responses from patients. [*]*, Theme;* [**]*, Subtheme.*

Providers also recommended the use of a brief screening strategy to determine patient's level of cognitive dysfunction, to adapt behavioral intervention strategies to meet the needs of those patients on demand. One provider said "I try to assess who I'm with in terms of comprehension." Another provider thought of using clinical information to help screen participants level of cognitive dysfunction.

"I thinking about using like a questionnaire to figure out where people are at. I mean, if you see the client, you already have access to SMART [electronic health records], so if you have those tools, just a quick questionnaire, that you can fill out with the client and the answers will determine where the person is with mental health and with their addiction."

Accommodation Strategies

A variety of evidence-based cognitive dysfunction accommodation strategies were discussed with treatment providers and patients on MOUD. To increase patient's ability to pay attention, retain and recall information, participants highlighted that "any mixed method of presentation or use of handouts is helpful." A multimodal presentation of information was supported, including the use of brief verbal presentation of information (<5 min of the facilitator talking), followed by the use handouts, videos, group discussion, and/or hands-on demonstrations. For example, one patient on MOUD indicated: "It is a combination of paper material and a video; I think it's always better to have both. Hands-on is always helpful." A provider described it below:

"I would tell them about opioid receptors and I would use magnets to demonstrate how opioids transit in the brain. I had a little box and I had balls and I would use different color balls and say 'this is how methadone affects the brain,' this is how the naloxone mimics the opioids, and use a square box with a round ball to show how the receptors react differently. A lot of people are more visual so that way, ya know, they're not verbal, they are visual."

When discussing the use of video clips, it was consistently recommended to keep them short (<10–15 min) and to include a debrief of the topics discussed immediately following the video. For example, "Incorporating short clips in educational group, the more formats to present the information, the better." **One** patient on MOUD noted how videos help to recall information by saying "you're watching something and, in your mind, you keep looking at it and thinking about it, and you think about it afterwards too."

The use of simplified verbiage, catchphrases, and visuals were also recommended to be considered when developing handouts for patients to maximize their learning. Providers highlighted the importance of simplifying complex language for patients to better understand, as exemplified by: "so that they can relate to this broken-down version. I just really break it down a few pictures and there's like a lot of little things like catch phrases or slogans that catch their attention."

Other accommodation strategies to help patients with cognitive dysfunction focus on the information being presented to them that were supported for use in a drug treatment setting included the use of a written agenda, memory aids, a short (1–2 min) mindfulness meditation and/or breathing activity at the beginning of sessions, and the use of a formal closure at the end of sessions. One patient on MOUD mentioned that "anything you see or actually do, as opposed to just hearing, will help people remember a lot better."

Patients on MOUD supported the use of a written agenda to help keep them focused. For example, one patient indicated: "I think it's helpful, it helps me anyways and I can keep looking up there, and in my mind, I keep trying to remember what was put on that board and what we've talked about." A provider also noted how a written agenda can reinforce goals and that patients "feel more accomplished" in striving to meet those goals when they can see what they covered in the sessions. A brief mindfulness meditation and/or breathing exercise was also supported to help improve patient's ability to focus on presented material. *One* provider mentioned doing "meditation here [the methadone clinic] for a year, 5 min for every group and it was always successful; they were more receptive to me and the information." This was exemplified by:

"I think with my experience of running groups with these clients, I've been more surprised with how receptive the clients are to some of the things I was anxious about trying. The game group, meditation, I mean I've had big burly construction guys who love the meditation. So, I guess the only thing I would ask is to try! And if it doesn't work, adapt it for the next time."

Patients on MOUD consistently noted the use of memory aids to help them remember to take their medications and attend appointments. One patient said "the text message reminder would really help me remember to take it [medication]." Both patients and providers supported the use of an automated reminder system to inform patients of upcoming treatment protocols, such as monthly check-ins with a counselor. One provider specifically mentioned that "it would be feasible" to integrate text message check-ins into treatment protocols. The use of a formal closure at the end of sessions to help patients recollect on the information and set realistic goals to focus on for the next session was also recommended. Participants noted that this gives them the opportunity to engage if they did not feel heard throughout the session; "I like this because sometimes you have a chance to talk, if you're quiet most of the time or don't like talking in front of other people, giving an opportunity to talk at the end is better." A provider mentioned how they would "have them [patients] put out particular goals that they're trying to obtain, and confirm that that's what the goal is." For example, one provider indicated:

"At the end of the session, we would do a review of the material to show you paid attention and learned something or have been affected by something that someone said. And you'll find commonality and people will build off of it and we discuss themes of the day and the topic of the group and the themes of the day. Being supportive and giving back to one another and just the whole concept of not being alone and sense of community or family."

DISCUSSION

Research on the influence of cognitive dysfunction among people on MOUD is quite limited. Studies have shown that cognitive dysfunction may impede treatment outcomes among people on MOUD (10, 14); however, no studies have investigated which cognitive dysfunction accommodation strategies may be most useful and feasible for integration into behavioral interventions in a drug treatment setting. This study is novel in exploring the endorsement of specific accommodation strategies that may be optimal for maximizing treatment outcomes (medication adherence, retention in treatment, healthcare utilization) for persons on MOUD. Themes identified in this qualitative analysis indicated high rates of cognitive dysfunction among people on MOUD and support for the integration of certain specific accommodation strategies into behavioral HIV prevention interventions during routine drug treatment.

Key informants (drug treatment providers and patients on MOUD) endorsed specific accommodation strategies including: a brief mindfulness meditation at the beginning of sessions, memory aids to help patients remember information, going over group etiquette at the beginning of sessions, using agendas to keep participants on track during sessions, use of simple language and visuals in handouts, brief videos, hands on demonstrations, use of props and games, and use of closures focused on information reiteration and goal setting. Based on the success of these strategies in accommodating cognitive dysfunction among other patient populations with similar cognitive profiles, these strategies may enhance the efficacy of behavioral interventions by increasing patient's ability to learn, retain, and apply health behavior change information. Ideally, these strategies would be integrated into behavioral intervention sessions, and facilitated by drug treatment providers, to maximize participants' ability to engage in harm reduction behaviors.

Outcomes from this study can aid in informing future research to determine which of the proposed accommodation strategies may be most useful in compensating for (i.e., working around) the cognitive dysfunction often experienced by people on MOUD. Given the novelty of this area of inquiry, we recommend a series of future studies to investigate the impact of integrating these strategies on key outcomes among people on MOUD, including HIV prevention, overdose prevention, and retention in drug treatment. We recommend pilot work to test the feasibility of integrating these accommodation strategies into behavioral intervention sessions and to first determine the extent to which such strategies may boost outcomes. Although it is unclear whether certain individual or combinations of accommodation strategies might be most helpful among people on MOUD–given the diversity of cognitive profiles in this patient population-future research should examine key outcomes stemming from inclusion of a variety of combinations of strategies (e.g., Multiphase Optimization Strategy; MOST) (41). This research design would allow researchers to identify which combination of strategies most enhance patient's ability to process and utilize intervention content.

The present study provided analysis of what accommodation strategies were most supported by key stakeholders in a common type of drug treatment setting. We determined the preliminary acceptability of these accommodation strategies which provides an empirical foundation for further investigation/testing of selected strategies. While the outcomes from this study supported our concept of adapting accommodation strategies from other patient populations for use in a drug treatment setting, the efficacy of these strategies has not yet been examined among persons with MOUD.

CONCLUSION

The economic and societal costs of OUD have continued to increase in the U.S. in the past 20 years (42). Nearly one million people have died from an overdose since 1999 (43), and over 100,000 people died from an overdose in the past 12 months (44). Additionally, people who inject drugs accounted for 10% of new HIV infections in 2018 (45). Treatment for OUD utilizes behavioral interventions to limit these negative outcomes among people on MOUD and to reduce a range of health risk behaviors. As researchers continue to investigate methods to improve patient's ability to engage in positive health behavior change, cognitive dysfunction is an often overlooked limitation to behavioral interventions in persons on MOUD. In focus group interviews, both treatment providers and patients on MOUD endorsed various accommodation strategies to compensate for cognitive dysfunction. These accommodation strategies have the potential to increase the efficacy of behavioral interventions to reduce overdose, death, and HIV transmission among persons on MOUD, and are worthy of further investigation in future work.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by University of Connecticut Institutional Review Board. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

Material preparation, data collection, data analysis, and manuscript write-up were performed by CM and MC. CI contributed to the data analysis and final edits on the manuscript. The first draft of the manuscript was written by CM and all authors commented on previous versions of the manuscript. All authors contributed to the study conception and/or design. All authors have read and approved the final manuscript.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.