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Patterns, contexts, and motivations for polysubstance use among people who inject drugs in non-urban settings in the U.S. Northeast

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Abstract

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Research involving Human Participants and Ethical Approval: The Institutional Review Board at Brown University approved the study. All participants underwent informed consent process. Verbal informed consent was obtained from all participants.

BACKGROUND: Polysubstance use (i.e., using ≥2 psychoactive substances) is associated with increased morbidity and mortality and complicates drug treatment needs among people who inject drugs (PWID). We explored patterns, contexts, motivations, and perceived consequences of polysubstance use PWID in small cities and towns in the U.S. Northeast.

METHODS: Between October 2018 and March 2019, we conducted semi-structured interviews with 45 PWID living outside of the capital cities of Rhode Island and Massachusetts recruited online and through community-based organizations. Written transcripts were coded inductively and deductively using a team-based process and analyzed thematically.

RESULTS: All participants reported recent polysubstance use, with most using five or more classes of substances in the past three months. Polysubstance use often followed long personal drug use histories (i.e., years or decades of occasional drug use). Reasons for polysubstance use included obtaining synergistic psychoactive effects as a result of mixing drugs (i.e., using drugs to potentiate effects of other drugs) and managing undesirable effects of particular drugs (e.g., offsetting the depressant effects of opioids with stimulants or vice-versa). Polysubstance use to self-medicate poorly managed physical and mental health conditions (e.g., chronic pain, anxiety, and depression) was also reported. Inadequately managed cravings and withdrawal symptoms prompted concomitant use of heroin and medications for opioid use disorder, including among individuals reporting cocaine or crack as their primary “issue” drugs. Polysubstance use was perceived to increase overdose risks and to be a barrier to accessing healthcare and drug treatment services.

CONCLUSION: Healthcare services and clinicians should acknowledge, assess, and account for polysubstance use among patients and promote harm reduction approaches for individuals who may be using multiple drugs. Comprehensive healthcare that meets the social, physical, mental health, and drug treatment needs of PWID may decrease the perceived need for polysubstance use to self-medicate poorly managed health conditions and symptoms.

Keywords

Polysubstance use; Injection drug use; Opioid-related disorders; Opioid medication assisted treatment; Self medication; Rural health

INTRODUCTION

In the United States, unintentional drug overdoses caused 554,711 deaths between 1999 and 2017 (Centers for Disease Control and Prevention [CDC], 2019a). Although the majority of recent overdose-related deaths have been attributed to opioids, nearly two-thirds (62.6%) of fatal opioid overdoses have also involved other classes of drugs such as cocaine (34%), benzodiazepines (32.5%), and methamphetamine (12%) (Gladden, O'Donnell, Mattson, & Seth, 2019). Between 2012 and 2018, overdose deaths involving cocaine and other psychostimulants with abuse potential (e.g. methamphetamine and prescription stimulants [methylphenidate, amphetamine]) increased three- and five-fold, respectively (Hedegaard, Miniño, & Warner, 2020). Concurrent use of stimulants and opioids result in both cardiovascular strain and respiratory depression, thus increasing overdose risk and mortality (Glick et al., 2018; Turner et al., 2018). Concomitant use of opioids and depressant drugs, such as benzodiazepines, is also common and is associated with increased risk of fatal and

non-fatal overdose due to synergistic respiratory depression (Barocas et al., 2019; Jones, Mack, & Paulozzi, 2013; Park, 2017; Park, Saitz, Ganoczy, Ilgen, & Bohnert, 2015; Pizzicato, Johnson, & Viner, 2019).

The sharp increase in mortality associated with polysubstance use (i.e. concomitant use of two or more drugs) reflects an overall increase in polysubstance use in the U.S. over the past decade (CDC, 2019b; Jones, Logan, Gladden, & Bohm, 2015). For example, among individuals reporting past-year heroin use, 91.5% also used cocaine and 45.6% also used psychostimulants or tranquilizers in the same period (Jones et al., 2015). Similar patterns have been shown in diverse population subgroups, including women of reproductive age and veterans (Bhalla, Stefanovics, & Rosenheck, 2017; Jarlenski et al., 2017). In addition to presenting high levels of opioid use, the U.S. Northeast is the region with greatest increase of past-year cocaine use in recent years, making this region particularly vulnerable to negative health outcomes of polysubstance use (Barocas et al., 2019; Barocas et al., 2018; Hughes, Williams, Lipari, & Van Horn, 2016).

High levels of polysubstance use have also been observed among patients prescribed medications for opioid use disorder (MOUD), which is of concern because polysubstance use is shown to reduce retention in care and compromise the effectiveness of treatment for opioid use disorder (OUD) (Heikman, Sundström, Pelander, & Ojanperä, 2016; Wang et al., 2017; White et al., 2014). Use of multiple substances also complicates and limits therapeutic options for the clinical management of non-opioid substance use disorders (SUDs) and other mental health disorders due to increased risk of drug toxicity (McCance-Katz, Sullivan, & Nallani, 2010; Park, 2017). However, research including patients' perspectives on the relationship between polysubstance use and treatment of SUD, including MOUD, is lacking. Understanding the precise reasons for and contexts surrounding polysubstance use among patients prescribed MOUD or other medications is paramount to informing the development of mental health and SUD treatment services that are responsive to their complex needs.

Individuals coping with mental health conditions may use drugs to self-treat emotional distress and inadequately managed psychiatric symptoms (e.g., use of benzodiazepines without having a prescription to manage anxiety symptoms or stimulants to mitigate depressed mood) (Fatséas, Lavie, Denis, & Auriacombe, 2009; Kecojevic, Corliss, & Lankenau, 2015; Khantzian, 1985, 1997; Motta-Ochoa, Bertrand, Arruda, Jutras-Aswad, & Roy, 2017). For example, cocaine users in downtown Montreal described use of benzodiazepines without a prescription for coping with anxiety, sleep problems, and untreated pain (Motta-Ochoa et al., 2017). Polysubstance use may also help reduce undesirable effects of certain drugs (e.g., opioids for coping with stimulant-induced paranoia and agitation) or potentiate the psychoactive effects of drugs (i.e., sensation-seeking) (Fatséas et al., 2009; Kecojevic et al., 2015; Khantzian, 1997; Motta-Ochoa et al., 2017).

Recent literature examining motivations for polysubstance use has largely focused on non-prescribed use of prescription medications in urban populations (Allen & Harocopos, 2016; Lankenau et al., 2012; McLean & Kavanaugh, 2019; Motta-Ochoa et al., 2017). Few studies have investigated polysubstance use in less urban settings, where access to SUD treatment and other healthcare services may be more limited (Jarlais et al., 2015; Rosenblatt, Andrilla,

Catlin, & Larson, 2015). In addition to lower availability of healthcare services, demographic and socioeconomic characteristics (e.g., older populations, economic deprivation) in many non-urban areas of the U.S. contribute to a high burden of OUD in these settings, including the concurrent use of multiple types of opioids (i.e., prescription opioids, heroin and illicitly manufactured fentanyl, and combinations of these opioids) (Keyes, Cerdá, Brady, Havens, & Galea, 2013; Monnat, Peters, Berg, & Hochstetler, 2019). Furthermore, recent HIV outbreaks linked to injection of opioids and stimulants also underscore the need for in-depth research on polysubstance use in non-urban settings (Cranston et al., 2019; Peters et al., 2016). We thus sought to describe the patterns, contexts, and motivations for polysubstance use in non-urban communities across the U.S. Northeast, where prevalence of opioid (including fentanyl) and stimulant use and injection drug use are high and have risen in recent years (Barocas et al., 2019; Barocas et al., 2018; Hedegaard et al., 2020).

METHODS

Study design, setting, and procedures

We drew from a qualitative study on HIV prevention needs among people who inject drugs (PWID) in non-capital cities, small towns, and surrounding rural communities in Massachusetts and Rhode Island (two states highly affected by the nation's overdose crisis). Though average household income in Massachusetts and Rhode Island are above the U.S. average, the proportion of individuals living in poverty in some non-urban regions in these states is more than two-thirds higher than state averages (U.S. Census Bureau, 2020). Moreover, despite stable overall numbers of overdose deaths in Massachusetts and Rhode Island (CDC, 2018), opioid-related deaths and concomitant use of several types of opioids (i.e. prescription opioids, heroin, fentanyl, etc.) disproportionally affects non-urban regions of these states (Barocas et al., 2018; Monnat et al., 2019). Communities were selected for this study based on surveillance data indicating high levels of drug-related overdose deaths and HIV and HCV transmission.

Between October 2018 and March 2019, we recruited actively-injecting PWID (i.e., past 3-month injection drug use) who were ≥18 years of age and HIV-negative (via self-report) and spoke English, in partnership with community-based organizations (CBOs) providing health and social services to PWID (e.g., syringe service and drug treatment programs) and by placing ads on websites (e.g., Craigslist). Trained study staff conducted eligibility screening and informed consent procedures in private spaces within CBOs and participating research institutions. Participants provided verbal informed consent, which was documented by research staff, and received $25 for participation. All study procedures were approved by the Institutional Review Board at Brown University.

Data collection

Trained interviewers administered brief quantitative surveys on socio-demographics, drug use and injection-related behaviors (past three months), sexual behaviors, and healthcare utilization. Next, interviewers followed a semi-structured interview guide developed based on literature review and previous research with PWID (Bazzi et al., 2018; Biancarelli et al.,

2019) to ask open-ended questions on drug use, injection behaviors, sexual partnerships, physical and mental health needs, experiences with healthcare services, and acceptability of PrEP for HIV prevention (see Supplemental Materials). Although interview guides did not contain specific questions or probes focused on polysubstance use, it emerged in early interviews and regular team meetings as an important topic to continue exploring in subsequent interviews and team discussions. Interviews lasted 45-90 minutes and were audio-recorded and professionally transcribed.

Data analysis

Immediately following interviews, interviewers wrote brief reflections on key topics and emergent themes, which were then discussed in weekly team meetings in order to inform subsequent interviews, coding, and data analysis. To systematically code transcribed data, we followed a collaborative codebook development process (MacQueen, McLellan, Kay, & Milstein, 1998). First, after closely reading selected interview transcripts, team members developed a preliminary codebook containing deductive codes (i.e., based on key domains and questions in interview guides) and inductive codes (i.e., based on emergent themes such as polysubstance use). This codebook was iteratively tested and refined through independent application of codes to additional selections of transcripts. After finalizing the codebook through several rounds of this process, five members of the research team used NVivo (v.12) to double-code all interview transcripts. An investigator with extensive qualitative research experience then compared code application for consistency and led team discussions to resolve discrepancies and reach consensus through a negotiated agreement approach (Campbell, Quincy, Osserman, & Pedersen, 2013). The team recorded all coding discussions and decisions in a detailed log. After all transcripts were coded, the first author then reviewed data coded for “polysubstance use” (defined as concomitant use in the past three months) to identify themes in the data, which were discussed and further refined through team meetings (Braun & Clarke, 2006). Lastly, the first author created “analytic profiles” of participants so as to avoid over-fragmentation and decontextualization of qualitative data and integrate segments of data that are thematically related but appear on different parts of the interviews (Lekas, Siegel, & Leider, 2011; Siegel, Lekas, Onaga, Verni, & Gunn, 2017).

RESULTS

Participant characteristics

Among 45 participants, median age was 37 years (IQR=31-41 years; Table 1). The majority were male (n=29, 64%) and White (n=37, 82%), while nine (19%) identified as Latinx/Hispanic and two (4%) as Black/African American. Most were unemployed (n=26, 58%); 11 (24%) were disabled, and nine (19%) were employed at least part-time. Median weekly income was USD $200 (IQR=45-400).

Patterns of polysubstance use

In brief quantitative surveys, all 45 participants reported polysubstance use (past three months), and most (n=24, 53%) reported using five or more classes of substances (Table 2). As shown in Table 2, the substances most commonly used in the past three months were heroin or fentanyl (n=42, 93%), cocaine or crack (n=39, 87%), benzodiazepines (n=27,

60%), and methamphetamines (n=8, 18%). Use of legal substances (past three months) including cannabis (n=33; 73%) and alcohol (n=19; 42%) was also common. Seventeen participants (38%) reported currently using MOUD, 14 of whom were concurrently using heroin or fentanyl (with two concurrently using prescription opioids and one using cocaine and crack cocaine). Six individuals (13%) reported using MOUD to get high in the past three months.

Per our selection criteria, all participants reported injecting drugs in the past three months; of those reporting any opioid use (past three months), nearly all injected opioids in the period (n=43, 98%; including injection of heroin or fentanyl [n=42; 95%] and prescription opioids [n=4; 9%]). Among those who used cocaine and/or crack in the past three months, injection of these substances was also common (n=28, 72%). Six of the eight individuals reporting using methamphetamine had injected it in the past three months (75%), and two individuals using benzodiazepines in this period had injected it (7%). Injection of MOUD was reported by two of the 17 individuals who reported using this substance in the past three months (12%).

To help contextualize these high levels of polysubstance use captured in our quantitative surveys, qualitative interviews provided participants with an opportunity to explain which one or two substances or classes of substances were their main “issue drugs.” These were the substances that they liked the most, perceived themselves to be the most severely addicted to, or that caused the greatest problems in their lives, as explained by one participant:

> I use heroin and cocaine, smoke some pot [cannabis]. Hard drugs, yeah, heroin and cocaine, that’s it. (…) Heroin’s my worst. That’s my issue drug, I like the downs [depressant effect]. (41-year-old White man)

Contexts and motivations for polysubstance use

From qualitative interviews, the following five key themes emerged regarding the contexts and motivations for polysubstance use. First, participants described their personal substance use trajectories as influencing their current polysubstance use. Second, reasons for engaging in polysubstance use included managing the effects of other drugs and seeking complementary psychoactive effects. Third, participants also described their polysubstance use in the context of self-medication of physical and mental health symptoms. Fourth, management of craving and withdrawal symptoms also motivated polysubstance use, particularly MOUD in combination with opioids. Finally, participants described how cost and availability of specific types of drugs in their physical and social environments influenced their polysubstance use. Each of these main themes is described in detail in the sections below.

1. Drug use trajectories influencing current polysubstance use.—

Many participants discussed their drug use initiation and how their past drug use influenced current polysubstance use. Though the personal circumstances in which participants initiated drug use varied, many participants described years or decades of experimenting with multiple drugs before starting to regularly use or inject their current “issue drugs.” Therefore,

polysubstance use was often described as a gradual process from casual drug use to use of multiple substances and addiction:

> I started with weed. Alcohol, marijuana [cannabis], and then it progressed as time went on. Like, maybe in my 20s, I started sniffing cocaine at the clubs. (…) And then it progressed to smoking coke, shooting dope [injecting heroin], so by the time I was 32 I pretty much had done the coke, dope, now I'm shooting it. (45-year-old White woman)

2. Managing effects of other drugs.—For some participants, polysubstance use was a way to manage the effects of substances with opposing psychotropic effects, such as opioids taken right after or at the same time as stimulants (e.g., using opioids to come down from the stimulant effects of cocaine or crack, or vice versa, also in the context of "speedballs", i.e., using heroin and cocaine concomitantly):

> I would smoke crack and use heroin or fentanyl, what we call landing gear, to come back down. And once you get down, then you'll want to take another hit [of crack] to go back up, and it's just like a cat chasing its tail. It never ends. Go up just to come down, then go up [again]. (49-year-old Cape Verdean man)

More than simply balancing opposing psychotropic effects, some participants reported that combining different drugs could lead to synergistic effects (i.e., using drugs to potentiate the effect of other drugs), including for sex-enhancing or self-discovery purposes:

> Every girl I've ever slept with in my entire life, I've used drugs with. (…) Especially crystal [methamphetamine]. And then when you combine it with something like GHB [gamma-hydroxybutyrate], that's just the best ever, you know, as far as sex goes. But then [if] you want to go voyaging off into the universe, do a shot of crystal and special K [ketamine] in the same shot. It's amazing. (…) I don't know how to explain it. I feel like I've learned a lot about life in those kinds of experiences. (43-year-old White man)

Polysubstance use to obtain synergistic drug effects was also described in the context of combining stimulants, such as cocaine or methamphetamines, and opioids or benzodiazepines:

> Most people [are] just mixing it [drugs] up. The heroin with the cocaine [they] go hand in hand. And that's a high risk to OD [overdose] more than just shoot [inject] one drug, because when you [are] mixing it up, you [are] just putting two drugs in your body and sometimes your brain receptors don't know how to react when you put in too much of this or put in too much of that. Because the heroin is not that good [pure], actually, because it's not even heroin [it is contaminated]. [So] people try to make it stronger. And that's the way that maybe you can make it stronger, just [by] putting [mixing] cocaine. You actually can make the shot stronger, but that's a higher risk to getting OD. (33-year-old White man)

As discussed by the participant above, combining different classes of substances was perceived by some participants as posing greater health risks, particularly with respect to

overdose, which was also described in the context of combining two or more drugs with depressant effects, such as opioids and benzodiazepines together:

> I didn't know the risks of taking the Xanax [benzodiazepine] and dope [heroin] at the same time. And I [had] just come out of a [drug treatment] program, I [had] never OD'd [overdosed] in my life. (…) I end up coming out [of the program], I took a Xanax. I bumped into somebody, [and] they gave me like 60 fucking [bags of heroin] I was supposed to sell [and] I'm like, “Let me try it, one bag”. Fell out [overdosed], [received] eleven Narcans [doses of naloxone]. Eleven. (…) They hit me [with naloxone] 11 times, one was an IV, and I woke up. That was the first time I OD'd. (33-year-old Black man)

3. Self-medicating physical and mental health symptoms.—Stressful psychosocial events such as traumatic experiences and relationship issues with family, friends, or partners were perceived by many participants to have negatively impacted their mental health and facilitated polysubstance use. A participant who relapsed into heroin use when facing social problems and depression after many years of occasional use of alcohol and cocaine, explained:

> [For the past 10 years, I was using] nothing. Socially, yeah, maybe, but not habitual, all the time. It wouldn’t be every week or every night. Once every couple of months, I might do a little bit of cocaine, a few beers, you know, [with a] bunch of friends and that’s it, but not on an addiction scale, you know? (…) [Then] my car [got] stolen, just continuous problems, one after the other, you know? Depression leads to getting high, it’s all part of the reason to [get] high, you know. If you get any issues, problems, it’s an escape. (41-year-old White man)

Some participants reported using different classes of substances to “self-medicate” mental health symptoms that were not being adequately managed through the healthcare system. Facing unmet health needs, some participants described polysubstance use as a way to address their complex mental and physical health needs including anxiety and chronic pain:

> [I currently use] Suboxone [MOUD]. I also like to use Xanax [benzodiazepine], it calms me down. The Concerta, the Ritalin [prescription stimulants], gives me energy. I mean, of course, the Suboxone, takes away all the [pain]. 'Cause I also have chronic pain, and it does help, and that's mostly (…) just to make it through the day and not be in so much pain. (42-year-old White woman)

The participant above continued to explain that healthcare providers were not adequately managing their complex health issues, contributing to polysubstance use and having negative impact on interpersonal relationships, particularly with family members:

> I've had depression my whole life, but it hit more than anything when I got sick [chronic pain]. So my problem was just my pain. I need to function. I have a small child with autism, so I need to function during the day, and that's a lot of the reasons why I shoot up and everything. (…) I was diagnosed as bipolar [and] put on a lot of mental pills until they got me [to] where I was stable, but then it got to the point where it wasn't enough. (…) Something was missing. I wasn't getting the

> right thing to stabilize my moods during the day to get through, so I ended up trying heroin. (…) And then, after that, we [participant and husband] went to coke and that gave me a lot of energy (…) And then we tried crack and loved it [but] then it caused a lot of problems in my marriage, in my house (…) It destroyed my family.

In addition to perceived low availability of mental health care services in many non-urban regions, some participants perceived lack of mental health training among primary care providers to pose significant barriers to having their mental health needs met in the healthcare system:

> There's plenty of doctors, but I think a lot of it is located in [neighboring city]. There's not as much [many providers] located up here anymore. I am lucky that I still have my primary care [provider]. But what I wish that they would change is (…) to have to have a primary care doctor and a counselor and psychiatrist. It sucks because mental health up here is really hard to find, it just takes months to get in. And my doctor only knows so much. So it's like you gotta find people that are educated in all these different things because you can't just find in one person. And that's what makes health care around here difficult because everybody [every provider] does just one thing. (…) It makes me discouraged when it takes so long to get into a place [mental health service]. (29-year-old White woman)

For several participants, self-medicating mental and physical health issues with multiple substances enabled them to "function" and to "feel normal", but could ultimately worsen their health and social situations:

> I'm just trying to seek a way that I actually can function, like a medicine or something like that that actually can help me out, just to get through the day (…) Because sometimes, drugs for me [are] self-medicating, trying to avoid the pain. Most of the addicts will tell you the same. But their pain is still there, like you're just trying to avoid things (…) and actually, that's going to be worse when they use the drugs. (…) I'm just trying to function. Because when I don't got my drugs, I cannot function normal. I actually feel normal when I [am] on my drugs. (33-year-old White man)

4. Managing craving and withdrawal symptoms.—Some participants with current use of opioids described that concurrent use of MOUD helped reduce opioid use. In these instances, MOUD was helpful in managing cravings and withdrawal symptoms and, therefore, discouraged further use of opioids to avoid withdrawal syndrome:

> Some years into my youth, I got on methadone, but just for harm reduction, not for abstinence. And also to not have to deal with waking up sick [experiencing withdrawal symptoms] in the morning. You know, I'm not in my 20s anymore. It's not a fun adventure to have to wake up fucking sick every morning. (37 year-old White woman)

A few participants who were not using heroin or fentanyl also described MOUD as helping them manage cravings for crack, cocaine, and other stimulants. This is described by a

participant who used MOUD being prescribed for her boyfriend to manage her use of crack and other drugs:

> [I use] Suboxone. (…) I mean, I'm not a heroin user, but it's helped keep me sober from other things. It [suboxone] is prescribed for people that are typically heroin addicts, but for me, it helps with the crack cocaine and the K2 [synthetic cannabinoids]. It helps me, it gives me energy throughout the day, a nice consistent feeling throughout the day, too. It has multiple uses for me. (38 year-old White woman who reported using cocaine, crack, prescription stimulants and synthetic cannabinoids)

Some participants perceived that suboptimal doses or courses of MOUD prescribed by healthcare providers and inadequate management of OUD facilitated their concurrent use of opioids and MOUD. In some instances, perceived poor management of OUD led to discontinuation of MOUD or dropping out of detox programs:

> About a week and a half ago I was in a detox and (…) they stopped dosing me, so I left the program (…). If you don't get the heroin, you get sick, it's called dope sick [withdrawal syndrome] (…) [so] they had me on Subutex [MOUD] to prevent the physical withdrawals of heroin and the cravings. After three days, they stopped doing the Subutex and I was still pretty sick [feeling withdrawal] so I left the hospital. (53 year-old Black man)

Perceived suboptimal management of OUD was compounded by perceived lack of drug treatment services in non-urban locations. When existent, drug treatment services were not easily accessible and public or insurance-funded transportation services were often viewed as ineffective and disorganized:

> I go to the methadone [clinic] just because my insurance pays for my rides, and I really like the guy that's driving me. He's fought for me for a long time. Every day (…) I can just get in the car and (…) go dose, come back, and be dropped off. But some mornings [it doesn't work], that [transportation] company is doing so badly that they've gotten brought into court because they've gotten over 1,200 complaints since they started [to provide transportation to drug treatment]. You know, so most of the time, what makes me go to my clinic is because I have rides. But if I didn't, then, I [can't] get my dose every day. (31-year-old Latinx woman)

In addition to inadequate medical management of OUD, stressful life events, such as homelessness and bereavement, were barriers to consistent use of MOUD, leading to withdrawal symptoms and concurrent use of opioids. This is exemplified by a participant who was tapering off of methadone, missed appointments while experiencing homelessness, and ultimately relapsed:

> I [used to] go every day to a [methadone] clinic, [and] I was at a point where I was getting enough methadone, so I wasn't sick, and I stopped using [heroin]. And then I missed days [at the clinic], being homeless, I was out of the area, now I'm at such a low dose [tapering off methadone] that I still feel sick [withdrawal] in the evening and night. So I'll use [heroin]. (33 year-old White woman)

A few participants who were not interested in using MOUD reported using other drugs, such as cannabis and, less commonly, cocaine and psychedelics, to reduce their opioid use:

> I don't really use MATs [MOUD] unless you consider weed [cannabis] an MAT. Lately I've just been smoking [cannabis] like a chimney. I recently went to go live with my brother (…) [and] he comes home from work and smokes me up every day, and that's kind of helping me stay sober. (…) I'm not used to being sober all day every day, so the weed really helps. I rather prefer that [to] Suboxone [or] methadone 'cause I've heard that's just like synthetic dope [heroin] highs, so all that's going to do is make me want to use dope. (24 year-old Latinx man)

5. Drug cost and availability.—Cost and availability of certain classes of substances also had an impact on polysubstance use. A few participants also described how limited availability or affordability of specific drugs shaped their drug use, leading them to switch to substances that were more accessible in their communities, which included different classes of substances and MOUD:

> I started in February using crack, and then it got really expensive, so I switched over to heroin around, probably, March. And then around April I stopped (…) because I was getting Suboxone off the street at that time. [But now I'm getting Suboxone from a doctor], because [buying it off the street] was really expensive. (45 year-old White man)

As described above, the specific drugs some participants used depended on what was circulating in their communities. Therefore, a few participants reported changing substance use patterns when leaving communities (e.g., moving out or being incarcerated), as illustrated by a participant who regularly used crack before being incarcerated and then shifted to opioids upon release:

> [I'm using] mostly heroin and fentanyl. I mean, every once in while just a little bit of crack and coke, but shooting coke isn't really that big around here and smoking crack kind of it's gone with the wind now that the heroin epidemic took over. (24 year-old Latinx man)

The widespread presence of fentanyl and fentanyl analogs in the local drug supply, especially heroin, also influenced participants' experiences of polysubstance use. While a few participants believed they could access "pure" drugs (i.e., without fentanyl contamination) through specific drug dealers, most respondents presumed the heroin they were using could contain fentanyl. A few participants also described unknowingly using fentanyl-contaminated stimulants and benzodiazepines, leading to unintentional polysubstance use and increased risk of overdose:

> Every single close friend I had that was using opioids has died in the last two years. Everyone. The last one [friend who died] wasn't exactly an opioid overdose…The fentanyl killed him, but he bought Xanax [benzodiazepine]. We both bought the same ones and I took six [pills] and he took three and just one of the pills had too much fentanyl in it. We didn't know… And he died. (35 year-old White man)

DISCUSSION

In this qualitative study with PWID across non-urban settings in Massachusetts and Rhode Island, all participants reported recent polysubstance use, with most using five or more classes of substances in the past three months. Our findings, which detail the patterns, contexts, and motivations for polysubstance use, raise concerns about increased vulnerability to drug-related physical and mental health harms among people who use drugs in this region. In our study, the illicit drugs used most frequently were heroin and cocaine, which were often used together (i.e., as a "speedball"). These findings are aligned with U.S. estimates of cocaine use among people using heroin over the past decade (Jones et al., 2015). This combination of opioids and stimulants was described as helping manage psychoactive effects of these drugs. Antagonizing depressant effects of opioids with stimulants may lead to a false impression of tolerance and more frequent use of opioids, which could increase overdose risks (Glick et al., 2018). The concurrent use of opioids and other depressants such as benzodiazepines, which was also common in our study, dramatically increases the risk of respiratory depression and overdose and limits therapeutic options for managing SUD and other mental health conditions due to the possibility of harmful drug interactions (Park, 2017).

Similar to previous studies, we found the desire to "self-medicate" mental and physical healtconditions as an important driver of polysubstance use (Fatséas et al., 2009; Kecojevic et al., 2015; Motta-Ochoa et al., 2017; Vogel et al., 2013). Illicit substance use, including polysubstance use, may constitute maladaptive coping mechanisms to deal with emotional distress and other life adversities, but may ultimately result in deteriorating overall mental health (Khantzian, 1985, 1997; Sullivan, Edlund, Zhang, Unützer, & Wells, 2006). Participants' non-prescribed use of substances to cope with mental health symptoms is also an indication of barriers to accessing mental health services among PWID. Even though Rhode Island and Massachusetts have one of the highest ratios of provider per population in the U.S. (Young, Chaudhry, Pei, Arnhart, Dugan, & Snyder, 2017), there is a significant shortage and underutilization of specialized and mental health services outside of the major metropolitan areas in these states (Kirby, Zuvekas, Borsky, & Ngo-Metzger 2019; Patel, Huskamp, Busch, & Mehrotra, A. 2020). Furthermore, polysubstance use may interfere negatively with patient-provider relationships (Bohnert, Zivin, Welsh, & Kilbourne, 2011), creating a reinforcement system where unmet mental health needs lead to polysubstance use, which in turn threaten access to mental health services. Therefore, mental health services should promote harm reduction approaches in developing inclusive, trusting patient-provider relationships with clients regardless of current substance use (Hawk et al., 2017). As such, provision of comprehensive mental healthcare to PWID may be key to addressing polysubstance use (by reducing the need to self-medicate) and improving mental well-being. For example, integrated care models including fast access to primary care, case navigation, peer support groups, and specialized mental health services, such as psychiatric care, have shown promising results for management of substance use and mental health disorders among youth in North America, although rigorous evaluations of mental health outcomes are needed (Henderson et al., 2017; Henderson, Hawke, & Relihan, 2018; Settipani et al., 2019).

Future research should further evaluate comprehensive health care services for individuals engaging in polysubstance use with mental health comorbidities.

Considering the close relationship between mental health disorders and physical pain (Gatchel, 2004), health services for individuals engaging in polysubstance use must consider chronic pain management. Recent clinical guidelines highlight the importance of judicious prescription of painkillers in order to prevent opioid misuse (Dowell, Haegerich, & Chou, 2016). However, more stringent criteria surrounding opioid prescribing may also result in inadequate pain management for some patients, possibly influencing attempts to self-medicate physical symptoms with polysubstance use (Pergolizzi Jr., Raffa, & LeQuang, 2016). This concern is particularly relevant given that providers may hold personal biases against minority patients when considering prescribing opioids in clinical settings and that stigmatization of PWID in healthcare settings is common and may reduce the quality of care received by this population (Basilico, Bhashyam, & Heng, 2018; Biancarelli et al., 2019; Van Boekel, Brouwers, Van Weeghel, & Garretsen, 2013). Future studies should examine the impact of recent guidelines and changes in opioid prescribing on chronic pain management and polysubstance use among PWID and individuals with SUDs.

A specific type of self-medication identified in our study was the use of non-prescribed MOUD to manage cravings and withdrawal symptoms. MOUD, such as methadone and buprenorphine, are highly effective in the treatment of OUD, with substantial evidence that MOUD reduce opioid use and drug-related harms (Connery, 2015; Fullerton et al., 2014; Gjersing & Bretteville-Jensen, 2018; Langendam, van Brussel, Coutinho, & van Ameijden, 2001; Thomas et al., 2014). Self-management of cravings and withdrawal symptoms are the most commonly reported motivation for use of MOUD without having a prescription, highlighting potential barriers to accessing and adhering to these medications through healthcare services (Allen & Harocopos, 2016; Fox, Chamberlain, Sohler, Frost, & Cunningham, 2015; Lofwall & Havens, 2012; McLean & Kavanaugh, 2019). Indeed, unavailability of drug treatment services and rigid service enrollment and participation requirements (e.g., frequent visits to providers and abstinence-only programs instead of adopting harm reduction approaches) pose significant barriers to widespread uptake of MOUD in the U.S., particularly in rural areas (Lofwall & Havens, 2012; McLean & Kavanaugh, 2019; Rozanova et al., 2017). Inadequate MOUD dosing, programs that fail to take into account individuals' needs and expectations, including with respect to treatment goals (e.g., abstinence or reducing drug use), and attempting to gain autonomy over one's own therapeutic plans have also been associated with non-prescribed use of MOUD and polysubstance use (Hawk et al., 2017; Heikman, Muhonen, & Ojanpera, 2017; McLean & Kavanaugh, 2019; Rozanova et al., 2017). The development of harm reduction-oriented, patient-centered models of MOUD provision may help address use of MOUD without a prescription. For example, a patient-centered buprenorphine induction strategy with greater emphasis on self-management of MOUD and initiation of therapy at home (rather than on-site) was associated with greater reductions in any drug use among patients with OUD (Cunningham et al., 2011). Improving access to quality drug treatment services may also have an indirect impact on polysubstance use by reducing demand for non-prescribed MOUD, which is often sold by patients being prescribed these medications to obtain illicit drugs (Allen & Harocopos, 2016; Launonen, Alho, Kotovirta, Wallace, & Simojoki, 2015).

Future studies should evaluate the role of patient-centered drug treatment services and other forms of promoting access to MOUD in improving access to and retention in drug treatment services and levels of polysubstance use among individuals with OUD.

Barriers to healthcare services disproportionally affect individuals living in non-urban areas, where availability of healthcare services, including drug treatment, is more limited and where stigma and discrimination against PWID tends to be greater (Browne et al., 2016; Rosenblatt et al., 2015). The existence of political opposition and challenges to secure steady funding for SUD treatment and harm reduction services in many non-urban settings also constitute challenges to establishing longitudinal health services targeting PWID's needs in these communities (Edmond et al., 2015). Moreover, existing services in non-urban settings often lack specialized SUD treatment and "wraparound services" to address individuals' social and health needs (Edmond, Aletraris, & Roman, 2015). Wraparound services are health and social services that are not directly related to SUD but that may impact patients' access and adherence to SUD treatment, such as housing assistance, food subsidies, child care services, and HIV and HCV prevention and treatment (Etheridge & Hubbard, 2000). Wrap-around services may also directly influence structural determinants of health risks related to polysubstance use and SUD, such as poverty, homelessness, and social marginalization (Bourgois, 1998). Therefore, development of broad support systems that encompass health and social services and focus on individual, social, and structural determinants may help address polysubstance use, particularly in non-urban areas facing economic deprivation and lack of infrastructure to manage PWID's complex health and social needs (Rush & Urbanoski, 2019; Wang et al., 2019). To that effect, structural interventions addressing socioeconomic factors such as homelessness and unstable housing, unemployment, and low income, may contribute to decrease health risks associated with injection drug use (Aidala, Cross, Stall, Harre, & Sumartojo, 2005; Richardson, Mammel, Milloy, & Hayashi, 2019; Sherman, German, Cheng, Marks, & Bailey-Kloche, 2006).

Our study has several limitations. First, given that we purposively sampled PWID living in non-capital cities, towns, and surrounding rural areas of the U.S. Northeast, our findings may not be transferable to other, more urban populations. However, considering the unique patterns of drug and polysubstance use in non-urban areas of the U.S. and the dearth of qualitative studies with non-urban PWID, we believe our study addresses an important gap in the literature (Pear et al., 2019; Rigg & Monnat, 2015). Second, our venue-based recruitment in collaboration with CBOs may have resulted in our sample being comprised of individuals with more connections to available health and social services. As such, our findings regarding high unmet needs for mental health and drug treatment services may underestimate actual needs among PWID in these communities. Finally, since the primary focus of our interviews was HIV prevention including pre-exposure prophylaxis (PrEP) among PWID, we did not sample in order to reach thematic saturation related to all social or structural forces surrounding polysubstance use. Although we believe that our study provides important insight into some of the patterns, contexts, and motivations for polysubstance use among PWID in the U.S. Northeast, future research is needed to further characterize how factors such as gender, race, ethnicity, housing status, access to health and social services, and other social determinants of health shape polysubstance use behaviors, consequences, and intervention needs among PWID in this and other settings.

In conclusion, our study identified high levels of polysubstance use in a socially marginalized population of PWID. As polysubstance use may increase the burden of adverse health outcomes experienced among PWID, efforts to address it are urgently needed. Such efforts will require understanding the patterns, contexts, and motivations for polysubstance use. In particular, we identified distinct motivations for polysubstance use related to individual desires and self-medication practices that should be considered in the development and delivery of clinical and public health and interventions to treat and reduce harms related to polysubstance use. Physical and mental health and drug treatment needs of PWID are complex, so integrating polysubstance use disorder treatment into existing health and social service infrastructure at the community level (e.g., through sexual health clinics and CBOs) may be a particularly promising strategy (Fauci, Redfield, Sigounas, Weahkee, & Giroir, 2019; Fox et al., 2015; Stancliff et al., 2012). These efforts to treat polysubstance use should incorporate both pharmacological and non-pharmacological approaches and rely on close collaboration with community stakeholders for improved outcomes. Concerted, multi-component approaches to addressing polysubstance use in the U.S. may also be crucial to curbing morbidity and mortality related to drug use in the country.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Sociodemographic characteristics of people who inject drugs living in non-urban areas in the U.S. Northeast (N = 45).

Location	**n (%)**
Massachusetts	33 (73)
Rhode Island	12 (27)
Age in years; median (IQR)	37 (30.5-40.5)
Race/ethnicity, (not mutually exclusive)	**n (%)**
White	37 (82)
Hispanic/Latinx	9 (19)
Black/African American	2 (4)
Other *	7 (16)
Gender	**n (%)**
Cisgender male	29 (64)
Cisgender female	16 (36)
Educational attainment	**n (%)**
Some high school	10 (22)
Completed high school or GED	14 (31)
Some college	15 (33)
Completed college	6 (13)
Employment status (not mutually exclusive)	**n (%)**
Employed full-time (30+ hours/week)	5 (11)
Employed part-time (<30 hours/week)	4 (8)
Unemployed	26 (58)
Disabled	11 (24)
Full-time student	1 (2)
Part-time student	1 (2)
Weekly income from all sources; median (IQR)	200 (45-400)
Sexual orientation	**n (%)**
Heterosexual or Straight	35 (78)
Homosexual or gay	1 (2)
Bisexual	7 (16)
Queer	1 (2)
Not answered	1 (2)

* "Other" race/ethnicities included: "Puerto Rican", "Spanish", "Cape Verdean", and "Jew".

Table 2.

Substance use behaviors among people who inject drugs residing in non-urban areas in the U.S. Northeast (N = 45).

Substances used, past 3 months (not mutually exclusive)	**n (%)**
Heroin, fentanyl, or another synthetic opioid	42 (93)
Cocaine or crack cocaine	39 (87)
Cannabis	33 (73)
Benzodiazepines	27 (60)
Alcohol	19 (42)
Medication for opioid use disorder	17 (38)
Prescription opioids	12 (27)
Crystal methamphetamine	8 (18)
Prescription stimulants	5 (11)
Other drugs not prescribed	7 (13)
Drugs injected, past 3 months (not mutually exclusive)	**n (%)***
Heroin or fentanyl or another synthetic opioid	42 (100)
Cocaine or crack cocaine	28 (72)
Crystal methamphetamine	6 (75)
Prescription opioids	4 (33)
Benzodiazepines	2 (7)
Medication for opioid use disorder	2 (12)
Prescription stimulants	1 (20)
Other drugs not prescribed	2 (33)
Frequency of drug injection, past month	**n (%)**
4 or more times a day everyday	14 (31)
1 to 3 times a day everyday	17 (38)
1 to 6 days a week	8 (18)
One day a month or less	6 (13)
Number of types of substances used, past 3 months**	**n (%)**
2	2 (4)
3	12 (27)
4	7 (16)
5	10 (22)
6	9 (20)
7 or more	5 (11)
Number of types of substances injected, past 3 months**	**n (%)**
1	14
2	23
3	6

Substances used, past 3 months (not mutually exclusive)	n (%)
4	2

*Percentage of individuals who reported injecting these substances among those who reported using these substances

**Classes of substances included: heroin or fentanyl; prescription opioids (e.g., oxycodone, hydrocodone); medication for opioid use disorder (e.g., methadone, buprenorphine); benzodiazepines; cocaine or crack cocaine; methamphetamines; prescription stimulants (e.g., methylfenidate, amphetamine); alcohol; cannabis; psychedelics (e.g., psilocybin mushrooms, dimethyltryptamine) and others (e.g., nitrates, sildenafil, sertraline, and synthetic cannabinoids).