The effects of opioid policy changes on transitions from prescription opioids to heroin, fentanyl and injection drug use: A qualitative analysis

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Research Article

Keywords: Prescription drug monitoring program (PDMP), opioids, prescription opioids, heroin, fentanyl, opioid prescribing guidelines

Posted Date: April 14th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1533528/v1

Abstract

Background: Beginning in the 1990s, non-medical use of prescription opioids (POs) became a major public health crisis. In response to rising rates of opioid dependence and fatal poisonings, measures were instituted to decrease the prescription, diversion, and misuse of POs including prescription drug monitoring programs (PDMPs), closing “pill mills” (unethical doctors or clinics that knowingly dispensed large amounts of pain medications knowing these medications were being misused and diverted) , disciplining doctors who prescribed an excessive number of POs, and the advent of abuse deterrent formulations of POs.

Methods: We conducted in-depth-interviews with people who use prescription opioids, fentanyl or heroin from a rural, urban and suburban area in three states, Connecticut, Kentucky and Wisconsin. Interviews with PWUO focused on how they initiated their opioid use and any transitions they made from prescription opioid use to heroin, fentanyl or injection drug use.

Results: The majority of participants reported initiating use with prescription opioids, which they used for medical or nonmedical purposes. They described needing to take more POs or switched to heroin or fentanyl increased. As more policies were passed to limit opioid prescription, participants noticed that doctors were less likely to prescribe or refill prescription opioids. This led to scarcity of POs on the street which accelerated the switch to heroin or fentanyl. These transitions increased risk of overdose and HIV/HCV infection.

Conclusions: A careful analysis of how and why people say they transitioned from PO to heroin or fentanyl reveals many unintended harms of policy changes to prevent overprescribing and diversion. They also reveal ways we can mitigate harms that have already occurred and treat people who use opioids with compassion and respect, not stigma and punishment.

Introduction

Beginning in the 1990s, non-medical use of prescription opioids (POs) became a major public health crisis. Between 1995 and 2010, both admissions to emergency departments and treatment admission for opioid use increased ten-fold [1]. Between 1999 and 2011, overdose (OD) deaths related to opioids increased 265% among men and 400% among women [2-4]. In 2009, an estimated one in seven US residents aged 12 and older reported past nonmedical use of opioids [5].

In response to rising rates of opioid dependence and fatal poisonings, measures were instituted to decrease the prescription, diversion, and misuse of POs including prescription drug monitoring programs (PDMPs), closing “pill mills” (unethical doctors or clinics that knowingly dispensed large amounts of pain medications knowing these medications were being misused and diverted) , disciplining doctors who prescribed an excessive number of POs, and the advent of abuse deterrent formulations of POs. State PDMPs were designed to curb opioid misuse and diversion by tracking scheduled medications prescribed by medical providers and dispensed by pharmacies [6]. PDMPs were predicated on the idea that

reducing excessive prescriptions among medical providers or overlapping opioid prescriptions from multiple providers would reduce the supply of POs available for diversion and nonmedical use [7].

Forty-nine states have implemented some form of PDMP. While there is some evidence that PDMPs were effective in decreasing physicians' opioid prescriptions, some researchers have raised concerns that PDMPs may have had the unintended consequences of increasing rates of heroin use and overdose[6, 8] [9-12]. In fact, some modeling studies predicted that the short-term consequences of PDMPs may be a shift to heroin and a subsequent increase in opioid overdoses, but that opioid use (including heroin use) would eventually decline as fewer people would initiate opioid use through a doctor's prescription or from POs bought on the street. However, opioid overdoses have continued to rise exponentially since 2013, reaching 100,000 overdose deaths in 2021 [13].

While there have been many causes for the increase in overdose deaths, escalations in heroin overdoses are temporally associated with decreased opioid prescribing, lending some support to the concern that policy changes may have caused PO users to switch to heroin or illicit fentanyl [14, 15]. Although the proportion of people prescribed opioids who switch to heroin appears to be small, research has found that individuals who use PO nonmedically may shift to heroin use, particularly if they inhaled or injected POs [16-26]. Studies have shown markedly increased probabilities of heroin use after non-medical PO use compared to people who used PO only as prescribed, ranging from 19 to 40 times higher probabilities [20, 27].

Despite these strong temporal associations, research to determine the extent to which laws and drug reformulations to reduce the availability of POs caused the increase in heroin use are limited and findings are mixed. Some studies have found a positive association between state PDMP and heroin poisoning mortality, while others found no association [11, 28]. Other research found that the switch from PO to heroin use occurred prior to 2010 when most of the policy changes and drug reformulations occurred [14, 29-31]. Similarly, quasi experimental studies comparing overdose prior to and after reformulation of POs have found little short-term evidence that reformulation affected overdose rates beyond a shift in the types of opioids involved in overdoses [32, 33]. A longer-term analysis of the effects of reformulation found that overdose increased dramatically in areas more exposed to Oxycontin reformulation (i.e., those markets with a higher proportion of Oxycontin users). Few studies have asked people who use opioids non-medically whether they switched to heroin and their reasons for doing so, although some qualitative research suggests that abrupt discontinuation of a PO led to their transition to heroin [34]. Reasons why POs were discontinued are relatively unexplored.

Further, the relative price and availability of POs may have changed, in part, after implementation of the PDMP and other policies. Indeed, much qualitative research has found that participants mention the greater accessibility and lower cost of heroin compared to POs as reasons for their transition to heroin [19, 23, 35-37]. While to our knowledge, no research has compared the price of POs before and after implementation of policies to reduce opioid diversion and misuse, research has found marked decreases in the price of heroin over the past two decades [30, 38]. The street price of heroin has been

lower than $600 per gram every year since 2001, with costs of $465 in 2012 compared to $1237 in 1992 [38]. Unick and colleagues found that a $100 decrease in the price of a pure gram of heroin resulted in a 2.9% increase in the number of hospitalizations for heroin overdose [30]. Further, heroin has spread to regions of the US that did not formerly have heroin markets, particularly along interstate highways, although more remote, rural counties still tend to be characterized by PO use [39].

Research has also identified changing routes of administration among people who use opioids, from taking POs orally to sniffing or injecting them, or from sniffing heroin or fentanyl to injecting it [16, 26, 36, 40-43]. This transition might also have been a result of the relative scarcity and high price of POs after implementation of the PDMP and other policies, as sniffing or injection increases the efficiency of absorption, creating a more intense "high" for users. In fact, the ability to sniff or inject oxycontin and other POs was found to increase its abuse potential and led to the aforementioned policy changes and abuse deterrent formulations [44, 45]. Any increase in injection drug use can also increase the chances of drug overdoses and transmission of hepatis C virus (HCV) and HIV [46, 47].

In this paper, we use trend theory as a framework for understanding the transitions of people who use opioids from non-medical PO use to heroin or injection drug use, and the role that changes in policies to reduce PO prescribing and diversion played in these transitions. Trend theory examines the characteristics of people who use drugs (PWUD) and historical changes, including changes in drug policy and drug distribution systems, to explain and potentially predict changes in drug use over time [48-50]. Trend theory uses a combination of in-depth qualitative research, epidemiological data and material about the historical context to explain changing drug patterns [50]. We apply trend theory to qualitative interviews with people who use opioids (PWUO: PO nonmedically, heroin or fentanyl) in rural, urban and suburban areas of three states, Connecticut, Kentucky and Wisconsin. Examination of participants' transitions from medical to nonmedical PO use, from nonmedical PO to heroin or fentanyl, and their changing routes of administration reveal the effects of policy change on opioid use over time.

Methods

Study Overview

The current study is part of a larger project that aims to compare the factors that influence the effects of opioid-related laws and policies in Connecticut, Kentucky and Wisconsin on the transitions from prescription opioids to heroin, fentanyl, and/or injection drug use. An urban, suburban, and rural area was selected in each state to examine the role of the local context on these transitions. Study teams in each state conducted in-depth, semi-structured interviews with two groups: key informants and people who use heroin or prescription opioids nonmedically. The current paper draws from interviews with participants who use heroin, illicit fentanyl or PO nonmedically. Initial participants were recruited from harm reduction services or upon entry to drug treatment facilities that were identified in key informant interviews. Subsequent participants were referred to the study by PWUO who were interviewed through snowball sampling. Eligibility criteria included being 18 years or older and misusing prescription opioids

or using fentanyl or heroin in the past 6 months. PWUO were compensated $35 for completing in-depth interviews. We conducted 61 in-depth interviews with PWUO in Connecticut, 32 in Kentucky and 56 in Wisconsin.

Interviews with PWUO focused on how they initiated their opioid use and any transitions they made from prescription opioid use to heroin, fentanyl or injection drug use. Participants were asked how they started PO use, whether it was prescribed to them or not, and whether their initial use was for medical or nonmedical purposes. We also asked whether they ever used heroin or fentanyl, and to describe their first use and what led to the decision to use heroin or fentanyl. We asked them to describe their routes of administration (orally, sniffing or injecting) and whether that changed over time. For those who were initially prescribed opioids by their doctors, we asked if there was ever a time when a doctor refused to write a prescription or pharmacists refused to fill it and the reasons for this. Finally, we asked participants about the relative price and availability of different kinds of PO, heroin and fentanyl on the street, whether and how price and availability have changed over time, and what they thought the reasons for these changes were.

Data Analysis

All interviews were transcribed verbatim. We used a collaborative approach for data analysis. To develop a coding tree, we selected a transcript which the multi-state research team read to develop a preliminary list of codes. The preliminary coding list was then applied to three additional transcripts—which were purposively selected to reflect different experiences (e.g., state in which the participant lived, rural or urban location)— and refined until the research team reached consensus on a final list of codes, their meanings, and the procedures for assigning them to text data. The research team then used MAXQDA software to apply the final list of codes to the transcripts. The coding was completed by six members of the multi-state research team. Coding, the development of new codes, and memoing (jottings done by coders to capture relationships between codes or initial hypotheses) were tracked by the six-person team. We used bi-weekly team meetings for troubleshooting and quality checks that included the principal investigator of the study. We also read each transcript to summarize the person's drug use trajectory, including the drug that initiated their opioid use (particular PO, heroin), and whether they changed route of administration or drug of choice over time. These transitions were examined and compared across participants to develop the model presented below.

Results

As can be seen in Table 1, a large majority of participants (134/140, 90%) started with prescription opioids, used either medically or nonmedically. Roughly half of participants started with opioids that were prescribed to them (64/134, 48%). The majority of those who started with POs (111/134, 83%) switched to heroin, fentanyl or some combination over time, although fewer than half of participants in rural Kentucky reported switching (9/20, 45%). The lower proportion of those who used heroin or fentanyl in rural Kentucky may be a result of reduced availability of heroin in these regions, although participants

reported that heroin and fentanyl were widely available. In this paper, we focus on those who initiated their opioid use with POs.

Table 1
Summary of participants who initiated with prescription opioids (PO) and transition to heroin/fentanyl by geographical location (n = 149)

		Initiated with PO		Of those who initiated with PO, prescribed		Of those who initiated PO, obtained other way		Of those who initiated with PO, transition to heroin/fentanyl	
	Total	**%**	**(n)**	**%**	**(n)**	**%**	**(n)**	**%**	**(n)**
Connecticut	60	82%	(50)	46%	(23)	54%	(27)	90%	(45)
Urban 20	20	95%	(19)	36%	(7)	63%	(12)	100%	(19)
Suburban 20	20	70%	(14)	50%	(7)	50%	(7)	86%	(12)
Rural 20	20	80%	(16)	53%	(9)	47%	(8)	67%	(14)
Kentucky	32	94%	(30)	37%	(11)	63%	(19)	63%	(19)
Urban 12	12	83%	(10)	50%	(5)	50%	(5)	100%	(10)
Rural 20	20	100%	(20)	30%	(6)	70%	(14)	45%	(9)
Wisconsin	56	96%	(54)	56%	(30)	44%	(24)	87%	(47)
Urban 20	20	95%	(19)	68%	(13)	32%	(6)	89%	(17)
Suburban 20	20	100%	(20)	40%	(8)	80%	(12)	90%	(18)
Rural 16	16	94%	(15)	60%	(9)	40%	(6)	80%	(12)
Total 149		90%	(134)	48%	(64)	52%	(70)	83%	(111)

Figure 1 shows a sequential model with key transitions and ways that the PDMP, abuse deterrent formulations and other laws and policies affected these transitions to nonmedical use, different modes of ingestion and heroin/fentanyl. As mentioned, most participants initiated opioid use with POs, not heroin or fentanyl. These POs were either for a medical (pain) or nonmedical reason (recreation/to get high) and could have been prescribed to them or not. An example of an opioid that was not prescribed but was used for a medical purpose could be a friend giving the participant an opioid for back pain, while an example of a prescribed opioid used for a nonmedical purpose is using more of a prescription than needed to control pain and feeling the euphoric effects. Some participants reported being prescribed POs for several months or years. Others described immediately seeking out more opioids for a nonmedical reason after taking an opioid for the first time. Use increased with increased tolerance because their current dose did not control the pain, or because they “liked the way prescription opioids made [them] feel.” In such cases, participants described seeking out more opioids either through being prescribed

more, obtaining opioids from friends or family members who had them, or buying them on the street. Some participants were prescribed higher doses or more pills from their regular doctors over time. Others described doctor shopping to obtain prescriptions and using multiple pharmacies to fill them. Still others went to “pill mills” in Florida or found local “crooked doctors” who were willing to prescribe large quantities of opioids. Buying POs in the street or using heroin to supplement POs that were prescribed to them created a vicious cycle for participants, as they often had to take what was available, which could be POs of different doses or strength, or heroin or fentanyl, which could vary in purity.
The PDMP, new prescribing guidelines, drug resistant formulations, and increased media coverage gradually changed the ease with which participants could obtain POs from their doctors and the availability of POs on the illicit drug market. Participants reported that this was a process that started around 2010 until 2016 rather than a sharp divide between before and after implementation of these policies, perhaps reflecting media coverage and increased concern over PO misuse before policy changes, and delays in when PDMPs were implemented. State PDMPs have also changed over time, often moving from more voluntary to mandatory use [51]. Interviews with people in charge of developing and implementing the PDMP in each of our study states talked about changes over time moving from encouraging physicians and prescribers to register with the PDMP to mandatory checking of the PDMP when prescribing or dispensing any opioid (Author pub., blinded for review). PWUO reported changes in physicians’ prescribing practices that occurred gradually over time, centering around the time PO restriction policies were initiated. Many participants reported that their physicians cut off their prescriptions, often abruptly, for any of the following reasons: the patient had other drugs in their urine drug screens; the acute need for the prescription ended and doctors felt that participants no longer needed POs; the participant reported to the doctor that they were becoming addicted to the PO; or the doctor cut the prescription because of interactions with other drugs, particularly benzodiazepines. Participants also reported that doctors were less willing to prescribe POs to treat pain, particularly for patients with documented opioid use disorders (OUD) or patients on medications to treat opioid use disorder (MOUD), i.e., buprenorphine or methadone. These prescribing practices led to fewer POs available “on the street”, i.e., in the illicit market which, in turn, led to higher prices. In response, participants reported changing their routes of administration to sniffing or injecting POs, which allows more efficient absorption, switching to heroin or fentanyl, which was cheaper and more accessible than PO, or stopping or slowing down their opioid use. Sniffing and injection increases risk of overdose, while injection also increases risk for infectious diseases like HIV and HCV. Some participants reported going to detox to slow down their opioid use, buying buprenorphine or methadone on the street, or entering MOUD treatment. However, after a period of time in treatment and particularly after detox, if relapse occurs it carries a heightened risk of overdose.

In what follows, we will provide examples from interviews for each of the points in the model.

Initiation and Escalation of PO Use

As mentioned above, participants described starting PO use for medical and non-medical reasons and obtained their first POs through prescriptions written for them by their doctors, through friends or family

members or, less frequently, by buying them illicitly.

Some participants reported being prescribed POs for long periods of time, from several months to 20 years. POs were used for legitimate pain that was caused by serious accidents or illnesses. However, over time, participants reported needing higher doses and looked outside regular prescriptions to control their pain, like the participant below who was prescribed POs for twenty years.

Participant: I'm 56 years old. I would say 20 years, I was 25 years old when I started using them because I had back issues. I started on Tylenol 3. Then… I got hurt and they put me on…Percocet. I can't remember. There's so many different ones I was on I can't count…. I was on morphine, 10 milligram morphine…

Interviewer: Was there times where you, they kept raising the milligrams?

Participant: They went from five, then they went up to 10 milligrams. That's why they gave me Percocet. Then they gave me the morphine pill. I've been taking them for so long I started abusing it because my body was getting immune to it. I had to get more and I was running out. I had to go on the street and go buy them. It just got, over the years I spent a lot of money, thousands of dollars. I gave away jewelry for pills; whatever I can do to get a fix, put it that way, to get opiates, a pill, pain pills (Male, White, suburban WI, 56 years old)

Many participants described that the POs gave them a high in addition to controlling pain. As their tolerance increased, the pills no longer produced euphoric effects along with controlling the pain as the participant below describes.

Participant: When I first started out with it, it was I'd say either right on or maybe not enough because it was a lot of extreme pain, 9 broken ribs and a broken bone in my neck alone that just was a lot of pain. But after a few months, it started to become more of a feeling of just—the pain wasn't there at all. If I took my medicine the way I was supposed to, I was perfectly fine, if not better than fine. And I started having that feeling, which I know now was the feeling of being high (Male, white, urban CT, 31 years old)

Many participants were surprised that they became addicted to POs and were not aware of the signs of dependence. In part, this stemmed from the ease and frequency with which doctors prescribed, who no doubt believed the pharmaceutical claim that POs were not addictive if used to treat pain [52, 53]. Some participants confused withdrawal symptoms with continued pain from their injuries, as the participant below described.

Participant: I had to go through physical therapy to kind of learn how to walk again and deal with all that stuff. And after I was out of physical therapy and I'm walking again, I'm starting to feel better. It was just this feeling like I still have the pain…. So, I would take the painkiller and come to find out, I wasn't really in that much pain. It was like normal pain or not even pain at all. It was the fact that they were lowering my dosage so really what I was feeling was the withdrawals from being on the prescription medicine so long that when they came down from 30 mg to 15 mg, it's a big jump for the body to have been on it for 11 or 12 months, and then all of a sudden, we're going to drop you down halfway, like cut it in half completely.

So, I didn't know that at the time. I know that now because I've talked to people, I've learned about this. Like I said, I've tried to go to treatment, so I know that that's what it was. It wasn't really pain. It was more the detox feeling (Male, white, urban CT, 31 years old).

Pain pills took away both emotional and physical pain, making them almost irresistible to participants who had been through traumatic experiences.

Participant: The first time I was introduced to pain pills was, I was 18 years old, I was in a really bad car wreck. I went through the windshield, actually, and I had seven reconstructive surgeries on my face. And it was right when Oxycontin came out, and that was supposed to be the cure all drug. You weren't supposed to be addicted to it. Doctors were pushing it. And for about two and a half years, over my seven surgeries, I was prescribed Oxycontin 80 [mg], well, it had worked up to Oxycontin 80. It not only numbed the pain, but it numbed everything. I loved it. It became my best friend. You know, being 18 and literally not having a face, and being so uncomfortable with that, and just all the emotional pain, and physical pain, and all of that, it just numbed it all. I had found my very best friend. (Female, White, urban KY, 40 years old)

Some participants who were prescribed POs for short-term pain reported feeling high at first use and immediately sought it out to use nonmedically.

Interviewer: Describe for me the first experience using prescription opioids and what it was used for?

Participant: I believe the first time was in eighth grade, and it was because I broke my leg. And I can't remember what it was [particular PO] but oh my God, it was great. I took one and lied to my mom. I'm like, "Hey, just leave that bottle in here, just in case it doesn't work and I need to take another one." And I took three or four more. And oh, I was like floating on my bed, ooh. It was just like everything was too good, too bright. Nothing mattered….

Interviewer: Did you run out of the pills before time, that first time?

Participant: Yes, I actually went to my friend because I know he had pain pills. And I told him, "Hey, I tried this. Do you want to try it with me?" And we had a sleepover and we exchanged a bunch of pain pills (White male, suburban WI, 46 years old)

Some participants described being prescribed POs that they didn't really need or for a longer period of time than they needed. In many of these cases, participants immediately felt the high of POs and were motivated to continue to use.

Participant: First time I ever used opioids for recreation, recreational uses, is I was about 19, and I had never been addicted to anything. And when I started dating this guy, and he was addicted. And he warned me. He begged me not to start, and I done it anyway. And it was a 2 milligram Lorcet. They prescribed it to me for cleaning my teeth – of all things, a tooth clean…. And I snorted it…. I really wasn't addicted to them. I was just young and stupid and trying to be part of the crowd. It was just me trying to catch up to everybody else, I guess. Trying to be normal because, back then, that was the normal thing to do around

here. There's nothing else to do, so everybody starts getting high. And at the time, you'd get pain pills for anything, any reason. Have you ever heard of getting your teeth cleaned and getting pain pills for getting a tooth cleaned? (White female, rural KY, 41 years old)

Because of the over-prescription and abuse of PO, the participant above knew how POs were taken recreationally and sniffed it at first use.

Other participants described using POs medically but never received a prescription. Often, participants were given opioids by friends, partners or family members. The woman below borrowed pain pills from her boyfriend after cutting her finger in a work accident because she didn't have insurance.

Participant: I was in my early 20s… I was working in a kitchen. It was my first real job as a cook outside of school… I ended up cutting the tip of my finger off while chopping up bacon my second week in… I didn't have insurance at the time, so they wouldn't, it wasn't worth even prescribing me, so they just didn't because I couldn't afford it. And my boyfriend at the time… he threw out his back and he ended up getting a bunch of medication for it, muscle relaxers and Vicodin. He had a severe addiction to opioids at the time that I was aware of, but not the full extent until much later. So no, he didn't want the Vicodin. He told me it was because he just wants to stay away from it, blah, blah, blah. But it turns out later, the real reason, they weren't strong enough for him. So, he gave them to me to hold onto right around the same time I hurt myself, and I'm like, "Okay, he's not gonna take them, I might just have one here, just see what it is." The first time taking it, oh my gosh, all the pain went away. (White female, suburban WI, 23 years old).

Medical use without a prescription was facilitated by the large number of POs being prescribed with easy access to left-over medications. This also facilitated nonmedical use, as some participants described initiating opioid use as adolescents from family members' supplies or from friends who had taken family members' prescriptions.

Participant: Pain pills were never hard to find at the time. Even being young and being in school, all my friends knew somebody who could get them, or I had friends that stole them from their family medicine cabinet. I had friends that had older people that sold them the pills. I had a cousin who had access to, God, I don't even know. (White male, urban KY, 25 years old)

Importantly, the participant above states that POs were still easy to obtain up to 2012, well after the KY PDMP was established.

Less frequently, participants initiated opioid use from POs they bought on the street. Again, this was a function of the easy access to PO that came with over prescribing.

Participant: Well, first time I ever used prescription opioids, I was 15. I got them off the street, basically – back then, you could…. It was Lorcet…. It was on the street down here in town, on the street – back then, you could run around on the street and do pretty much anything. (White female, rural KY, 42 years old).

Increased tolerance

Almost all participants reported a time in which they needed to take more POs to control their pain or to get high. All described taking POs to avoid withdrawal. While some continued to get POs from their doctors, others used more than what their physicians prescribed. Obtaining more could be accomplished through prescriptions from pill mills, doctor shopping or finding “crooked” doctors who were willing to prescribe large quantities of POs. Those who went to pill mills or doctors, in turn, sold POs to other users and on the illicit market.

Participant: They called it the pill pipeline, people were driving to Florida, getting prescriptions and then driving back with them. They were the people that were basically taking people, they were giving them their money and having them go up, get their prescriptions and then they got the packs…. So, they had a little business going on for a little while. (White female, urban KY, 30 years old).

Interviewer: So, when you first tried it, how did you get it?

Participant: I got it through one of my friends. He had a dirty doctor. He got caught [the doctor]. He was just laying out, you know, here’s a couple hundred dollars, and he would write you a prescription for whatever. Anyway, I was buying them from my buddy that was getting them from him. (White make, suburban WI, 34 years old)

More often, participants reported buying POs on the street. As this participant describes, supplementing their legitimately prescribed POs with those bought on the street often led to increased tolerance as participants were limited in what they were able to buy to what was available on the street, which often was a higher dosage or different type of opioid.

Participant: That’s what sucks, is like I’m only on 10 mg oxycodone, and only 30 mg morphine. In the beginning I got, I think it was 90 morphine. But I have weaned myself down on that, and my doctor’s helping me wean down on oxycodone, which is good. But anytime I run out, I can’t find little 10 oxycodone that I’m on and that’s the thing. I would always get like a 30 mg or something, and I’d try to cut that in half, whatever. Because every time that I end up taking more than I’m prescribed, then I’m addicted more. And when I get my normal script back from my normal doctor, it’s not enough. (White male, suburban WI, 43 years old.)

Increased tolerance was particularly true for participants who used heroin to supplement their medical or nonmedical use, as heroin quality and strength varied considerably as will be described in more detail below.

Changing landscape: PDMP, pill mills and drug reformulation

While some participants weren’t aware of changes in laws or policies and simply noticed that POs on the street were becoming scarcer over time, others directly experienced some of the changes and their effects on PO availability and price. One such change was the closing of “pill mills” that were a source of some POs sold illicitly in Kentucky and Connecticut.

Interviewer: What have you heard about legal efforts to limit prescription opioid supplies?

Participant: I was just watching the news on that. Anywhere, you have to be on your death bed to get pain pills. Like I said, in Florida, everybody got busted.

Interviewer: What would people go there to get?

Participant: Anything and everything. The oxycontin, the Lortabs, everything for pain. They would get somebody's address in Florida or something and go to the doctors. And they would give them a 90-day prescription. Somebody would pay for the trip and give them so many pills. And they'd get the rest of them or something. Everybody, the doctors, and everybody got busted in Florida. And people that were doing it got busted. That's why I thought everybody couldn't find pills anymore. (White Female, urban KY, 53 years old).

Others noticed that doctors were no longer prescribing opioids which they attributed to increased media coverage of PO abuse, disciplining physicians who over-prescribed and the PDMP.

Participant: Say, I got kidney stones or something or anyway that you know how to do it to get it. But now they're really strict. Now, with the computer situation everybody knows everything. Every doctor you go see, they know what you're on. I don't care what doctor you see now, they know. Back in the day, you can go to three different doctors and get three different medications and they don't know. But now with the computer age, it's everywhere. (White male, suburban WI, 53 years old).

Many states' PDMPs require prescribers and dispensers to report opioid prescriptions to the PDMP immediately, which is then available for everyone with access to the database, including everyone who has registered (physicians, APN, PA and pharmacists in the three states studied here). This makes it easy for prescribers to check whether participants have been "doctor shopping" and have received prescriptions from more than one doctor.

Many participants who had been prescribed opioids for long-term pain were cut-off by providers after the changes in law, often abruptly, with little consideration for tapering or prescribing MOUD or referring patients to drug treatment. The participant below describes how his doctor made him take urine drug screens after repeatedly trying to fill his prescription early. After finding a medication in his urine drug screen that he wasn't prescribed, he was cut-off with a very abrupt taper.

Participant: Well, no, she found a medicine in my system that wasn't supposed to be in a drug test and right then and there, she was like, "Okay, we're going to start weaning you off of it." And it literally was within a three month period that I went from taking I don't know, 150 mg of Percocet a day…10 mg of Valium and maybe 15–20 mg of Vicodin to taking 75 mg of Percocet, 5 mg of Valium, everything was cut directly in half. And then the very next month, it was cut in half one more time and the very next month, there was absolutely nothing. And I've talked to so many clinicians and many people and treatment centers that told me that was just completely unsafe to wean somebody off that had been on painkillers and that high of a dosage for two years to just wean them off in three months and then expect there to be

no habit or no repercussions. So, I'm not saying it's all her fault. It's partially the system's fault. It's my fault for going and buying what I was buying and abusing other drugs, but it definitely could've been done a different way. (White male, urban CT, 31 years old)

Another participant who had been prescribed high doses of POs for over a year was cut off abruptly after he started taking buprenorphine to manage his withdrawal symptoms as he was being tapered off opioids by his doctor. When the doctor found out that he had taken buprenorphine, he was immediately taken off POs without referrals to drug treatment.

Participant: They started to [taper me] a little and then they kicked me off because I went and got some Suboxone [buprenorphine] one day 'cause I was really sick, so I went to detox for a couple days and then I – so I could lower my dose, so I wouldn't be so sick and then I went back and got pills for a week and then the doctor found out I went there and she cut me off. I said but you've been giving me them…. I'm addicted to these things….so I had no choice but things I didn't want to do….

Interviewer: So, they just kind of found out that you got on the Suboxone?

Participant: Well I told'm [that I took buprenorphine] and I said you can't just cut somebody off like that. It made me sick. You can't do that to a man. They pushed me down the road to dope. Like I said, I wasn't selling them for dope but I did a little bit just to stretch it and then they pushed me to it really…

Interviewer: Yeah. So, did they—did your doctor provide or recommend any alternative for you when they cut off your prescription?

Participant: No. She's like, "Go back to where you got the Suboxone," being a smartass. That's all she could say. I think it's messed. I said I'm gonna be wicked sick. I said this is messed up and they didn't care (White male, rural CT, 45 years old).

Another participant talked to a doctor about her concerns that she was misusing POs. The doctor cut her prescription immediately without tapering or referral to MOUD or a drug treatment program.

Participant: At the age of 25, I want to say it was 25, 26, I actually came out and told my doctors that I was addicted to the pills and I was abusing them. They took me off, weaned me off and transitioned me to just doing Tylenol and Motrin.

Interviewer: From Vicodin to Motrin and Tylenol?

Participant: From Percocet at that point… Yeah, because I told them I had a problem with it. But I found myself still withdrawing from them because I had taken them for so long. I couldn't sleep or anything, so I started buying on the street (Hispanic female, urban CT, 33 years old.)

Only one participant in our study had a doctor ask if they wanted to go to a drug treatment program after refusing to prescribe an opioid.

Participants also reported that doctors wouldn't prescribe opioids to them even for acute pain incidents because the patient's medical charts indicated they had been prescribed MOUD or that they had an OUD. This occurred even in cases in which the source of pain was easily observable, and POs were customarily prescribed, like a broken arm, stab wounds or post-surgery.

Interviewer: Have you ever been denied a prescription opioid?

Participant: Oh yeah, absolutely. Since I've gotten off them and I've been to the hospital a few times with some pretty bad injuries… Once it's on file that I've been to treatment centers and I'm considered an addict or I have been, whatever, they're not giving me nothing. Here take a Tylenol. I hope you feel better. It's like I have two cracked ribs, I don't' think Tylenol 3 is gonna do it but they don't want to give it you because you're on file as abusing pain medication so that's definitely happened to me a few times since….And it's like, to me that's not right. If there's a legitimate problem, then there's a legitimate problem. I can understand if someone's coming in off the streets complaining of neck pain, you do an x-ray and there's nothing on the x-ray, yeah okay. If there is something wrong, I feel like you should treat it regardless if the person has a past of opioid addiction or abuse because the bottom line is, it's one of very few things that helps that type of pain unless they figure out something that takes that pain away (White male, urban CT, 31 years old)

Doctors sometimes refused to write prescriptions if participants had been on MOUD even if they were no longer taking it. In other cases, they told patients that they were unable to prescribe opioids or other drugs that cause respiratory depression like gabapentin or benzodiazepines when a participant was on MOUD because it was contraindicated.

Fewer prescriptions on the street: transitions of route of administration and switches to heroin

Much qualitative research has found that PWUD reported switching from nonmedical PO use to heroin because it is cheaper and more accessible [36]. Similarly, qualitative research has demonstrated that PWUD often switch from taking POs orally to sniffing or injecting them, as this gives them an increased high [36]. Few studies, however, have shown how changes to reduce the prescribing of opioids led to scarcity on the street and increased price. It is in this context that many participants in our study reported switching to heroin or changing their route of administration.

Participant: So, one of my friends who had been helping me to get painkillers, he had been using for a little while and he had already talked to me about it a few times, like you really should stop wasting all your money buying these pills. You're running out of money and after a month or two when I really noticed that like my money was getting really low… and we wanted to go meet somebody for pills. The person didn't show up, something happened, and my friend was just in my ear. So we jumped on the bus, we came up here, he brought me somewhere, grabbed it [heroin] and after that it was just all heroin because it was just so much cheaper and it had the same effect that painkillers had, if not stronger, more

intense in the beginning, if anything, so I just didn't care and that was it (White male, urban CT, 31 years old).

The participant above went on to describe that when he first used heroin, it was $3 a bag, which was equivalent to a 10 mg Percocet that would sell for $10.

Some participants described the increase in price as directly related to the scarcity of POs after changes in prescribing practices.

Participant: I've noticed that prescription opioids have skyrocketed all the way up to $2 a milligram. And since I've first tried heroin to present day, I think that, because I paid $40 the first time… I've only really seen or heard of that same amount going for around $60, tops, and it's rare. It's usually for $50. So, really, it only jumps like $10 in the last 10 years. With opiates, that's like doubled in price for the pills.

Interviewer: Right. Okay. Do you attribute that to the new laws, and policies, and stuff, that have been put in place?

Participant: Yeah, like they're cracking down, so people are more apprehensive to sell them if they've got them. And then, of course, you run into the scenarios where, you know, how bad do you need it? How much money do you got? Highest bidder kind of thing. And I've seen 60 milligram OxyContin go for $250. So, there's those rare occasions where there's a bidding war over the last available, and it gets pretty colorful. (White male, rural WI, 36 years old)

Participants described that using heroin created a vicious cycle of increased tolerance because it was stronger, and the quality could be variable. Similarly, injecting was described as creating a more intense high and was thought to increase tolerance and addiction.

Participant: So then we'd end up buying heroin because it's so much cheaper than pills. You can get a big bag of it, and it does more. And then, you snort it. Well, I was satisfied. I was happy. But I hated it because every month, then I'd have to go back to my normal pills after a week of doing heroin. And then, I'd be at a different level. So, then when I do my regular pills, it's not enough. So, I would feel horrible. You have to do a certain amount just to feel not sick anymore. But everyone does a little more than that. And that's why your tolerance keeps going up. (White male, suburban WI, 46 years old)

While most participants in the face of withdrawal or not being able to find POs described transitioning to heroin or injection or both, others decided not to transition fearing that they might die from overdose, or "never come back" from addiction, like the participant below, who would not transition to heroin.

Participant: Well, I mean, I've had – when I went to get something that I wanted and they didn't have it, they'd say, "Well, no, we have heroin. Do you want to try it? It's real good. It gives you a good buzz." I – "No, I don't because I've had a few friends overdose on heroin. I've had a few friends die from overdosing on heroin and I just don't want to go there." That's one I don't want to – I would never try it. (White female, rural KY, 53 years old)

Access to Syringes

The prescription opioid crisis affected cities and regions that had a history of heroin use as well as areas where heroin had never been used. In the northeast, cities like Hartford, CT had a long history of syringe exchange programs (SEP) and law and policy changes to allow the buying of syringes without a prescription in pharmacies to prevent HIV and HCV transmission. Some larger cities in the Midwest, including Milwaukee, also had long histories of SEP services. Participants in Milwaukee and Hartford reported that syringes were easily accessible and few reported sharing. However, in both Connecticut and Wisconsin, a new challenge was providing these services to suburban and rural areas. In Kentucky, SEPs are more recent and the decision to allow and provide SEPs are made county by county. To make matters worse, participants in rural areas in Kentucky and Wisconsin reported that pharmacies that had been selling syringes stopped as the opioid crisis escalated and more PWUD were injecting drugs.

Interviewer: What was some of the reasons that you had trouble getting them [syringes]?

Participant: You couldn't buy them at the pharmacy anymore and it just happened to us all of a sudden one day. We tried to go get some and then you couldn't get them anymore, this has been maybe five, six years back. At that time, after that, we had to share the same needle over and over and over again. I didn't know what to do. Now, with the needle exchange, if I needed it, it's there. (White female, rural KY, 32 years old)

Efficiently providing harm reduction programs in rural and suburban areas is challenging because of lower population densities and increased distances. Participants in the rural and suburban areas of both states reported that the hours and days SEPs operated were limited.

Participant: I'm glad it's there. I really am. I mean, there is so many people who didn't get it in time because they were only doing it once a week, one time. So, they only give you 10 needles at your first visit. And so, they was using those needles to death. So, they were getting infected in their arms because they were so gone, so they were getting really frustrated and couldn't hit their veins. So, they go ahead and shoot it in the skin, so it boils up and it's just gross. There was a whole lot of cases of that. I'm really glad that they have that program. (White female, urban KY, 53 years old)

Mobile vans that delivered syringes directly to participants helped resolve the difficulty in providing accessible syringes in less populated areas. Interestingly, the participant also describes the difficulty in obtaining syringes before the mobile SEP was available.

Participant: They deliver out here [in suburban area] on Monday. And they meet you wherever. I'm dead serious. So, I meet them like, "Hey, I'm here. Can you meet me here in a half hour or whatever?" Boom. "How many needles do you want? Do you want 10 or 20? … And the funny thing too was, when I first started shooting up, when I was 21… Walgreens, at first, they'd sell them to you. Then you had to show some kind of like, in effect, that you're diabetic or something like that…. And then it just completely cut

off. But now they sell them again. You can just go in there, and you know, tell them I want a 1 cc, 28 gauge, boom. And you can buy them there (White male, suburban WI, 34 years old)

Discussion

Results from this study provide evidence of unintended consequences of state PDMPs and changes in opioid prescription guidelines. Many participants described easy access to POs when they first started using opioids; they all reported that doctors were less likely to prescribe prescription opioids over time. Participants reported that doctors prescribed opioids for trivial disorders or long term. This easy access led to many POs being diverted to be illicitly sold on the street or used recreationally. Many participants became physically dependent and supplemented their prescriptions with pills they bought on the street, or less often, heroin/fentanyl. Over time, they noted that POs on the street became scarcer and their price increased as POs were prescribed less often. Under these circumstances, participants transitioned to other routes of administration (sniffing and injecting) or to heroin/fentanyl.

The PDMP and other policy changes that came about to decrease the overprescribing of opioids in the 1990s and early 2000s are historical events that changed the course of the opioid epidemic, albeit in unintended and harmful ways. Rather than decreasing opioid use, these policies instead appear to have caused at least some people who were initially prescribed opioids to transition to riskier drug use such as injection or using heroin/fentanyl. Although our participants do not represent the majority who were prescribed opioids for pain, most of whom take them only as prescribed and do not switch to heroin, the increasing rates of overdose deaths due to heroin and fentanyl suggests that the number of people who switched to heroin is not trivial. The existing market for POs on the street was replaced with heroin when POs became less available [54]. Trend theory is a useful framework for understanding these changes over time [50]. Importantly, while much policy research measures changes after implementation of the policy, change can be more gradual than usually assumed in such analyses.

It would be difficult and undesirable to eliminate the PDMP and other measures that are now in place to prevent over or inappropriate prescription of opioids. However, a number of steps can and should be taken to mitigate the negative effects of this change that we now see. Prescribing best practices should be accompanied with best practices for patients who misuse opioids, become physically dependent or develop an opioid use disorder (OUD). Physicians should assess whether patients who were prescribed opioids have developed OUD and offer them medication for opioid use disorder (MOUD) or refer them to opioid treatment programs (OTPs). Patients who misuse POs by refilling too early or taking other opioids bought on the street should not have their opioids abruptly discontinued. Similarly, patients who have been diagnosed with an OUD and patients on MOUD should not be denied medications to manage acute pain. Such actions are punitive and harmful as many patients may seek relief from pain or withdrawal with heroin or fentanyl. Further, these punitive actions are stigmatizing to people who use opioids as they suggest that people with opioid use disorder are untrustworthy or undeserving of relief.

It is estimated that less than 20% of people with OUD receive MOUD [55–57]. Research suggests that the low uptake of MOUD is driven by stigma [58]. There is great need to educate physicians, people who use opioids, and the community at large about the safety and efficacy of MOUD, and the dangers of detoxification and other contraindicated “drug treatments” that may decrease tolerance and increase overdose risk. There is also a need to increase community education about opioid misuse, overdose and its reversal and the benefits of harm reduction.

A careful analysis of how and why people say they transitioned from PO to heroin or fentanyl reveals many unintended harms of policy changes to prevent overprescribing and diversion. They also reveal ways we can mitigate harms that have already occurred and treat people who use opioids with compassion and respect, not stigma and punishment.

Abbreviations

HCV Hepatitis C virus

HIV Human Immunodeficiency virus

MOUD Medications to treat opioid use disorder

OUD Opioid use disorder

PDMP Prescription drug monitoring programs

PO Prescription Opioids

PWUD People who use drugs

SUD substance use disorder

Declarations

Ethics: Research presented in this paper was approved by the Medical College of Wisconsin, Institutional Review Board.

Consent to participate: Informed consent was obtained from all participants prior to interviews.

Consent to publish: All authors have read the manuscript and consent to its publication.

Availability of data and material: Data are available by request to the first author.

Competing Interests: The authors declare they have no competing interests to declare.

Funding: The research was funded by the National Institute on Drug Abuse (R01DA044971).

Authors contributions: JDG wrote the manuscript draft. SK, AS, DG and JO coded and analyzed data and AS, DG and JO conducted in-depth interviews. All authors read and commented on paper drafts.

Acknowledgments: We would like to acknowledge Juan Flores, Julie Cassidy, Sophie Boutouis, Eduardo Robles and Lucy Rohena for their help in recruiting and interviewing participants, and to all the participants who agreed to share their experiences with us.

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Tables

Table 1: Summary of participants who initiated with prescription opioids (PO) and transition to heroin/fentanyl by geographical location (n=149)

		Initiated with PO		Of those who initiated with PO, prescribed		Of those who initiated PO, obtained other way		Of those who initiated with PO, transition to heroin/fentanyl	
	Total	**%**	**(n)**	**%**	**(n)**	**%**	**(n)**	**%**	**(n)**
Connecticut	60	82%	(50)	46%	(23)	54%	(27)	90%	(45)
Urban 20	20	95%	(19)	36%	(7)	63%	(12)	100%	(19)
Suburban 20	20	70%	(14)	50%	(7)	50%	(7)	86%	(12)
Rural 20	20	80%	(16)	53%	(9)	47%	(8)	67%	(14)
Kentucky	32	94%	(30)	37%	(11)	63%	(19)	63%	(19)
Urban 12	12	83%	(10)	50%	(5)	50%	(5)	100%	(10)
Rural 20	20	100%	(20)	30%	(6)	70%	(14)	45%	(9)
Wisconsin	56	96%	(54)	56%	(30)	44%	(24)	87%	(47)
Urban 20	20	95%	(19)	68%	(13)	32%	(6)	89%	(17)
Suburban 20	20	100%	(20)	40%	(8)	80%	(12)	90%	(18)
Rural 16	16	94%	(15)	60%	(9)	40%	(6)	80%	(12)
Total 149		90%	(134)	48%	(64)	52%	(70)	83%	(111)

Figures

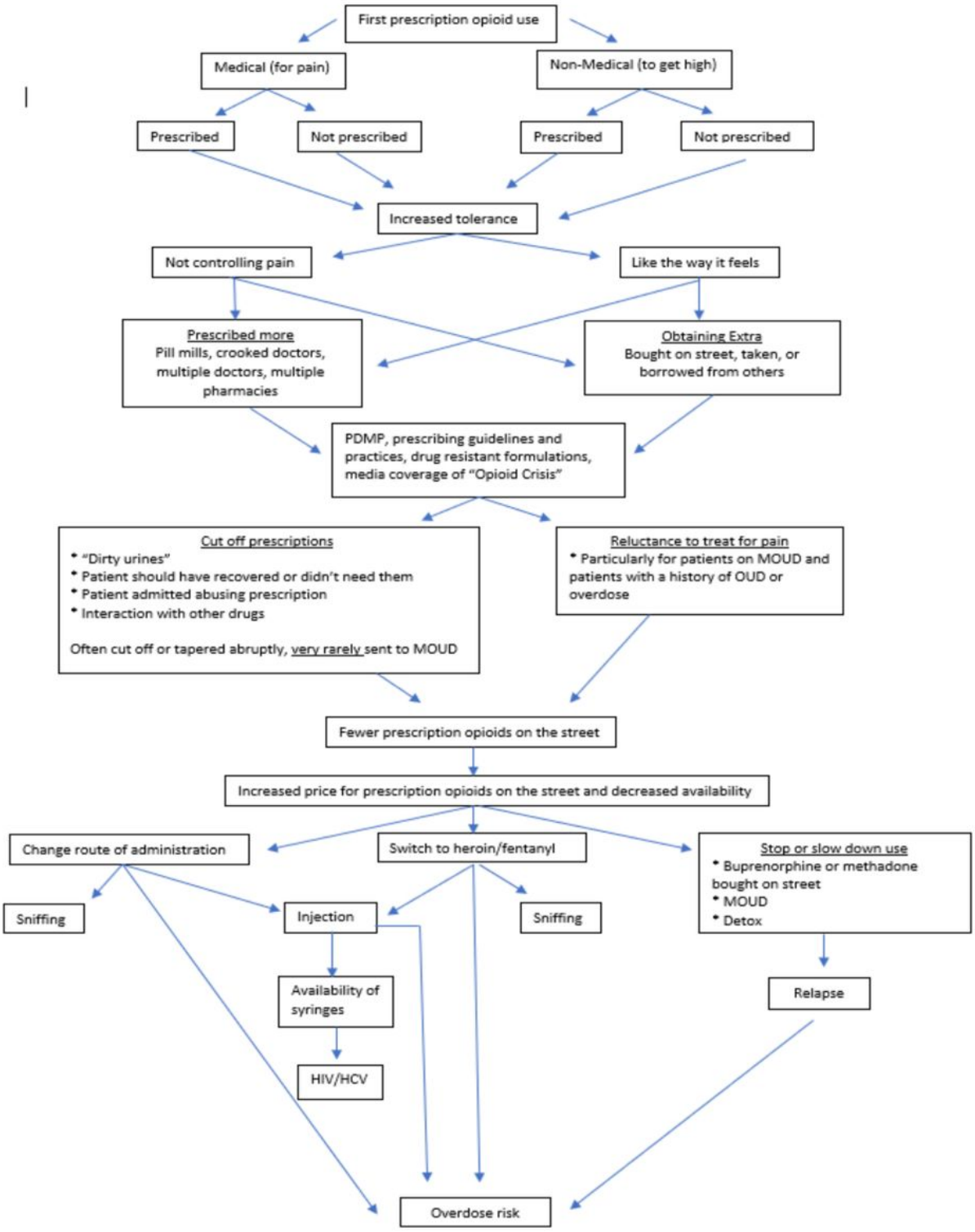

Figure 1

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