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Multiple injections per injection episode: High-risk injection practice among people who injected pills during the 2015 HIV outbreak in Indiana

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Abstract

Background: Misuse of prescription opioid analgesics (POA) has increased dramatically in the US, particularly in non-urban areas. We examined injection practices among persons who inject POA in a rural area that experienced a large HIV outbreak in 2015.

Methods: Between August-September 2015, 25 persons who injected drugs within the past 12 months were recruited in Scott County, Indiana for a qualitative study. Data from in-depth, semi-structured interviews were analyzed.

Results: All 25 participants were non-Hispanic white and the median age was 33 years (range: 19–57). All had ever injected extended-release oxymorphone (Opana® ER) and most (n = 20) described preparing Opana® ER for multiple injections per injection episode (MIPIE). MIPIE comprised 2–4 injections during an injection episode resulting from needing >1 mL water to prepare Opana® ER solution using 1 mL syringes and the frequent use of “rinse shots.” MIPIE

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Disclaimer

The findings and conclusions in this paper are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention, Indiana State Department of Health, the Indiana Campus Compact, Indiana University-Purdue University School of Liberal Arts, or Indiana University Richard M. Fairbanks School of Public Health.

Conflict of interest statement

None.

occurred up to 10 times/day (totaling 35 injections/day), often in the context of sharing drug and injection equipment.

Conclusions: We describe a high-risk injection practice that may have contributed to the rapid spread of HIV in this community. Efforts to prevent bloodborne infections among people who inject POA need to assess for MIPIE so that provision of sterile injection equipment and safer injection education addresses the MIPIE risk environment.

Background

Over the past 15 years, the use of prescription opioid analgesics (POA) has increased dramatically in the United States, particularly in non-urban areas, with a growing number of people moving beyond ingesting and insufflating pain pills to injecting them (Cicero, Surratt, Inciardi, & Munoz, 2007; Paulozzi, Mack, & Hockenberry, 2014; Rudd, Aleshire, Zibbell, & Gladden, 2016; Surratt, Kurtz, & Cicero, 2011; Young & Havens, 2012). Increases in the number of people who inject drugs (PWID) have contributed to dramatic increases in incident hepatitis C virus (HCV) infections, with young PWID (age < 30 years) comprising a majority of new cases (Suryaprasad et al., 2014). Diagnoses of HIV infection among PWID have been steadily decreasing since peaking in the 1990s, due largely to effective prevention efforts for PWID. Yet recent HIV surveillance data suggest behavioral and demographic trends associated with the opioid epidemic may threaten these earlier successes (Van Handel et al., 2016; Wejnert et al., 2016). Injecting POA may further amplify these risks; there is growing evidence that persons who inject POA are at higher risk for HCV infection than persons who inject heroin and other drugs but not POA (Bruneau, Roy, Arruda, Zang, & Jutras-Aswad, 2012; Zibbell, Hart-Malloy, Barry, Fan, & Flanigan, 2014). Given that injection drug use is an important risk factor for both HIV and HCV infection, the findings of increased HCV risk associated with POA injecting also have serious implications for HIV prevention. The largest injection-related HIV outbreak to date in a non-urban region of the United States was linked to the injection of POA extended-release oxymorphone (Opana® extended release [ER] with INTAC®, hereafter Opana® ER) (Peters et al., 2016). These findings highlight the need for improved understanding of the types of opioid formulations being injected and the mechanics involved in preparing them for injection so that risk reduction interventions can be designed specifically for pill injection. At present, there is a paucity of data on injection practices and related health risks associated with pill injecting, particularly in non-urban settings. We present findings from a qualitative study conducted in Scott County, Indiana, the epicenter of the HIV outbreak, among PWID to examine the types of prescription opioids and injection techniques that may have contributed to the rapid dissemination of HIV in this rural community.

Methods

From November 18, 2014 to November 1, 2015, 181 new HIV diagnoses were made in Scott County, Indiana (estimated population, 14,799 persons aged 18–65 years in 2014) and HIV control and prevention measures were implemented, including a syringe services program (SSP) (Peters et al., 2016). The SSP (the first in the state of Indiana) was established on April 4, 2015, within one week of the Indiana Governor declaring a public health

emergency, and operated by Scott County Health Department. The SSP included both a fixed-site and mobile outreach services, with program participants provided one week's supply of sterile syringes based on the number of syringes returned and the reported frequency of daily injections.

In August-September, 2015, face-to-face, in-depth interviews were conducted with 25 PWID using semi-structured, open-ended interview guides. Several convenience-sampling methods were used to obtain a wide cross-section of injection networks and representation by key characteristics (e.g., age, sex, HIV/HCV status), including recruitment in the SSP, street-based recruitment, and peer-driven referral. Eligible participants were ≥18 years, resided in Scott County, were able to complete the interview in English, and reported injecting drugs in the past 12 months. Drug injection was confirmed by examining physical marks of recent injection. Interviews with consented participants were digitally recorded, transcribed, cross-checked, and prepared for descriptive analyses using NVivo 10 software. To enhance rigor, two researchers analyzed data by independently reviewing transcripts and then comparing notes for inter-coder agreement. Transcripts were coded into broad categories and then subcoded into refined categories for detailed descriptions of injection practices.

The interviews were anonymous; no names or other identifying information were collected. Human subjects and ethics review and approvals were received for the study from the institutional review boards of the Centers for Disease Control and Prevention and Indiana University.

Results

Table 1 reports participant characteristics and self-reported HIV and HCV status. All 25 participants were non-Hispanic white: 11 were women and the median age was 33 years (range: 19–57). All participants reported having ever injected Opana® ER. Most (n = 22) reported injecting Opana® ER as their primary drug within the 12 months prior to the interview; 1 reported primarily injecting Opana® immediate release (IR), and 2 primarily injected methamphetamine. Ten participants were HIV positive and 21 were HCV positive.

In contrast to Opana® IR and the type of heroin and methamphetamine available in this rural part of Indiana, all of which dissolve relatively easily in aqueous solution, study participants described a multi-step process to prepare Opana® ER for injection (Table 2, a). To circumvent Opana® ER's crush-resistant technology (INTAC®), the pill was heated for several minutes in a conventional oven or, more commonly, directly in a cooker by applying heat to both the bottom of the cooker and the top of the pill. Participants referred to this process as "browning." Browning the pill made it malleable, softening it just enough so it could be crushed with the force of finger pressure. Participants described browning the entire 40 mg Opana® ER pill or, more commonly, a quarter of the pill. The cost of Opana® ER in this community was very high ($120–160 per pill) but reduced portions of the pill were available for purchase at $30–40 per quarter (10 mg). Participants reported that quarter portions were a more affordable option for most PWID in the county, which translated to quarter pills being the common dose used/shared during single injection episodes (Table 2, c).

Once the browned pill was sufficiently mashed, water was added to it in the cooker and the mixture was then manipulated with a finger or the back of the syringe plunger to further aid in dissolving the pill. Participants reported using between 1.2 and 1.7 mL of water volume for each quarter of a 40 mg browned pill. The outcome was an Opana-based solution whose total volume exceeded the volume that can be contained by a 1 mL insulin syringe, the syringe-type most commonly available and preferred by participants. To inject the entire solution during a single injection episode using a 1 mL syringe, multiple injections are required.

Most participants (n = 20) described the experience–their own or others'–of preparing multiple injections per injection episode (MIPIE), which involved administering two to four injections during a single injection episode, often with the same needle/syringe (Table 2, b). MIPIE was reported as a common practice involving both "multiple loads" and "rinse shots." Multiple loads consist of several injections being derived from a single drug solution whereby each shot is considered a separate "load." Rinse shots involve adding water to the pill residue in the cooker and/or filter after the entire pill solution has been injected via multiple loads to extract any remaining drug. In contrast to heroin, whose salt form dissolves quite easily in aqueous solution with little to no residue, participants injecting Opana® ER reported ample pill residue in the cooker after the entire solution was removed, which they believed contained unextracted oxymorphone. The rinse shot may be injected immediately or saved for later. MIPIE was described to occur both before and after the community became aware of the county's HIV outbreak. Only one participant who injected Opana® ER did not report MIPIE. MIPIE was rarely described for drugs other than Opana® ER (e.g., heroin) (Table 2, b).

MIPIE was performed in two specific ways: either one person injected him/herself multiple times to consume the entire solution and a "rinse shot" during a single injection episode, or the solution was distributed to multiple persons who injected together during a single injection episode whereby each person received an individual "load" or a "rinse shot" (Table 2, c). MIPIE often occurred in the latter context with injecting partners sharing injection equipment (e.g., syringes, cookers) to prepare, apportion and inject Opana® ER. Syringe reuse and sharing were less commonly reported after the SSP opened but the sharing of ancillary injection equipment (e.g., cookers) and the apportioning (e.g., backloading) of Opana® ER solutions among multiple persons via syringes continued. This is likely due to the consistently high reported cost of Opana® ER, both before and after the SSP opened, and the need participants described to pool money to purchase and thus share Opana® ER. MIPIE occurred multiple times daily (up to 10 injection episodes/day) leading to a high number of total daily injections per person (up to 35 injections/day) (Table 2, d).

Discussion

To our knowledge, this report is the first to describe MIPIE among persons injecting POA in a non-urban setting in the United States. Our most notable finding is that people using Opana® ER in Scott County, Indiana are performing MIPIE and administering a larger aggregate number of daily injections than has been typically described among persons injecting heroin (Magura, Kang, Nwakeze, & Demsky, 1998). MIPIE occurred before

and after participants' knowledge of the HIV outbreak and often in the context of many injection episodes performed daily with multiple injecting partners who shared pills and reused injecting equipment. Of concern is the possibility that MIPIE facilitated the rapid dissemination of HIV infection through this injecting community and could continue to pose challenges to ongoing prevention efforts.

MIPIE is occurring because > 1 mL volume of water is required to prepare an aqueous Opana® ER solution for injection using a 1 mL insulin syringe, the most common syringe used by PWID in the US. The explanation for why participants need to prepare such high-volume solutions lies with the abuse-deterrent mechanism included in Opana® ER, INTAC®. INTAC® employs a high molecular-weight polyethylene oxide that produces high resistance to crushing of the tablet for insufflation or injection in combination with hydroxyl-cellulose, a gelling and thickening agent, to enable the extended release of oxymorphone. The extended release mechanism operates by swelling and forming a viscous gel in the presence of liquid in the gastrointestinal track that through diffusion and erosion steadily releases active drug. When PWID mix Opana® ER with water in a cooker to prepare an injectable solution, the ensuing mixture turns similarly viscous and becomes too gelatinous to inject (Cicero, Ellis, & Kasper, 2016). To circumvent this process, extra water is added to generate a more liquefied solution that can effectively be drawn into a syringe. Participants in this study using 1 mL insulin syringes reported needing between 1.2 and 1.7 mL of water to produce this outcome with Opana® ER; henceforth the need for multiple loads. Further, contrary to unadulterated heroin salt, which fully dissolves in aqueous solution, many prescription opioid formulations–not just Opana® ER–contain fillers and binders (e.g., talcum, a silicate mineral) that are insoluble in water and thus remain in the cooker as residue after the entire solution is removed. Participants injecting Opana® ER believed this residue contained unextracted oxymorphone, so to further ensure that no drug is left unused, water is added to the pill residue in the cooker and another solution–a "rinse shot"–is prepared and injected. In view of these findings, this study shows that the abuse-deterrent and extended release technology included in Opana® ER may be inadvertently placing people at increased risk for bloodborne pathogen infection when this formulation is diverted and injected.

MIPIE has been described in two qualitative studies in Montreal and New York City among persons who inject POA other than Opana® ER (Mateu-Gelabert, Guarino, Jessell, & Teper, 2015; Roy, Arruda, & Bourgois, 2011). Comparable to the rinse shots described by our study participants, both studies describe the preparation and sharing of "washes" or additional "shots" that result from adding surplus water to residue left in the cooker. Taken together, these findings suggest that MIPIE may be common practice among people injecting POA–beyond just Opana® ER–and could be contributing to higher overall frequency of daily injections and heightened risk for bloodborne disease transmission, as observed in recent studies that found a significant association between the injection of POA and increased risk for HCV infection (Bruneau et al., 2012; Zibbell et al., 2014). Of concern is that some PWID may perceive themselves as practicing safer injection techniques because they use a new, sterile syringe for each injection episode. Yet, if PWID share injection equipment (e.g., syringes, cookers, water) when preparing multiple injections, such as reusing the same syringe to prepare loads and rinse shots for themselves and their injecting partners, there is

potential for everyone's individual portion of drug solution to be contaminated even when a sterile syringe is used at the outset of the injection episode.

Public health implications

Due to the increases in the number of people who report injecting POA in the United States (Surratt et al., 2011; Young & Havens, 2012), these findings have immediate implications for prevention of HIV and other bloodborne pathogen transmission. MIPIE poses significant challenges for disease prevention because performing multiple injections during every injection episode presents added opportunities to re-use and cross-contaminate injection equipment, in addition to increasing a person's aggregate number of daily injections. Larger volume syringes able to accommodate higher volume solutions are not a recommended alternative to reduce MIPIE since they contain more "dead-space" (i.e., the space between the syringe hub and needle) and are proven to retain more fluid, including diluted blood, which can increase the risk of HIV and/or HCV infection if shared (Vickerman, Martin, & Hickman, 2013; Zule & Bobashev, 2009). Beyond syringes, the requirements necessary to prepare an injectable POA-based solution also affect the type of ancillary injection equipment that is needed. Because a higher volume solution is required to prepare POA for injection, a cooker/container than is larger than the type typically needed for preparing heroin for injection is also essential. Furthermore, many of the binders and fillers included in pill formulations are insoluble in water and injecting them can cause detrimental health problems, including embolism, if these particles are not removed through appropriate filtering systems prior to injecting (McLean, Bruno, & Brandon, 2009). It is therefore imperative that SSP staff and other prevention and health service providers working with people who inject POA probe thoroughly to identify MIPIE, both to ensure the appropriate provision of sterile syringes and to tailor safer injection education to the mechanics of pill injecting and the MIPIE risk environment. If a sterile syringe is not used for every injection during an injection episode, persons starting with sterile syringes may unknowingly cross-contaminate their injection equipment through multi-person sharing of drugs and/or injection equipment.

Since POA injecting is disproportionally occurring in non-urban areas (e.g., Appalachia) where sterile injection equipment may be scarce, secondary or satellite syringe services may be a viable option for ensuring that people with access to a SSP can provide sterile equipment and safer injection information to people in their injecting network(s) who do not. Effective strategies to reduce bloodborne pathogen transmission among people who inject drugs in non-urban jurisdictions such as Scott County will require novel comprehensive and integrated approaches that include expanding syringe access (e.g., mobile SSPs, peer-to-peer outreach, non-prescription pharmacy sales) coupled with affordable, evidence-based treatment for opioid use disorder (e.g., medication-assisted treatment). Over the last several decades, these interventions have been shown to be effective and cost-effective in reducing HIV and viral hepatitis risk. Ensuring these efforts are adopted and tailored to the risk environment associated with pill injecting will be key to further protecting the public health and saving lives.

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Table 1

Demographic Characteristics, Drug Injection, and Self-Reported HIV and HCV Status of Study Participants Who Injected Drugs during the 2015 HIV Outbreak in Rural Indiana[a] (n = 25).

Characteristic	n (%)
Age (years)	
19–29	*10 (40)*
30–39	*9 (36)*
≥40	*6 (24)*
Median (range)	33 *years (19–57)*
Race/ethnicity	
Non-Hispanic white[b]	25 (100)
Gender	
Male	14 (56)
Female	11 (44)
Ever injected Opana[c]	
Yes	25 (100)
No	0 (0)
Drug injection, past 12 months	
Currently injects	22 (88)
Injected in the past 12 months, but not currently	3 (12)
Primary drug injected, past 12 months	
Opana[b]	22 (88)
Immediate-release oxymorphone	1 (4)
Methamphetamine	2 (8)
Self-reported HIV status	
Positive	10 (40)
Negative	15 (60)
Self-reported HCV status	
Positive	21 (84)
Negative	4 (16)

[a] All participants were aware of the HIV outbreak in this community at the time of the interview.

[b] Race/ethnicity of participants reflects background race/ethnicity of the community (http://quickfacts.census.gov/qfd/states/18/18143.html).

[c] OPANA® ER with INTAC®, a proprietary formulation of extended-release oxymorphone with non-FDA approved abuse deterrent formulation.

Table 2

Multiple Injections per Injection Episode[a] and Related Drug Preparation and Injection Practices among Persons Who Injected Drugs during the 2015 HIV Outbreak in Rural Indiana[b].

Key Themes	Exemplar Quotes
a. Preparing drugs for injection	
Multiple steps to prepare Opana® ER for injection	Male, 34 years old: I cut it [Opana ER[c]] in half. I put it on a pop can. You take a lighter and you melt it, because it gels up if you put water on it. You take a lighter and heat it up, and burn the bottom of it, smash it down, and cook it again until it turns brown, and then cook the top of it a little bit and put about 150 units of water on it, and work it up with your finger. You'll see it start oozing out of the pill, black stuff starts oozing out. It [heat] kills the gel in it, that way you can draw it up. Take a piece of clean cigarette filter that has the cotton and draw it through that.
Multiple steps not required to prepare drugs other than Opana® ER	Male, 19 years old: I literally put [Opana IR[d]] in there [cooker] … put water on it … stir it up … draw it up, no heat. Male, 34 years old: You don't generally have to cook it [heroin] like you do an Opana [ER]. You just add water to it, keep working it, and it will eventually dissolve. Some of it [doesn't require heat].
b. Multiple injections per injection episode	
2–3 injections per injection episode	Male, 43 years old: Each pill [Opana ER] you get 2 to 3 shots off of each one. You can't get it all in one shot. I've put a quarter of a pill in a can and mix it the best I can. I draw it up. You got to put more [water] in there than what you can draw. A quarter pill you need more than 100 [units]. I mean, you can get by with 120, but its real thick. It's real hard to draw up, so you need to put about 150 on it. No matter what it's thick … You still have 50 left.
Additional 1–2 "rinse shots" per injection episode	Male, 43 years old: And then even after that [2 shots from a quarter of ER oxymorphone], you put more water on it and mix it some more because there's stuff left over. So, that's 3 shots right there. Just off a quarter piece. Some people rinse it more than once. They'll rinse it again. So, they're doing 4 shots.
Rarely described for other drugs	Male, 33 years old: One time and you're good, you know. If you've got decent dope [methamphetamine], you do a shot and you're good, you know… Heroin, I've seen people try to take, get three or four shots off of it, but you can't, you know, because heroin it's one shot and you're done.
c. Multiple injections per injection episode in the context of sharing drug and injection equipment	
Multiple drug sharing partners allows for at least "1 shot" and "1 rinse" per partner	Male, 34 years old: I just work half the pill [Opana ER] up in the can, because it's still hard, you have to take your finger and work it up, just leave about half of it on there and draw what you got, split that [with one other person]. And when we get done hitting that, we'll put more water on it, about 80 units of water on it and work it up and then split that.
Sharing due to the high cost of the drug	Male, 22 years old: One quarter [pill] is 30 dollars. It's very expensive… Every time she gets a pill, she shares with us. Every time we get a pill, we share with her. Female, 27 years old: We can't make enough money to get that quarter,… I've only made maybe $20, I'm short $15. There might be another person that's short the other 20, so we'll all get together, throw our money in together, and then we'll go do the quarter three ways.
Syringe and other injection equipment (e.g., water, cookers) sharing	Female, 40 years old: [Before the HIV outbreak] I'd go there's 14–15 people [in one house injecting]… Same needles and everything. There's people everywhere with cans, and needles, they'd share a cup of water.
Syringe-mediated drug sharing (i.e., "backloading")[e]	Female, 37 years old: Many times [before the HIV outbreak] there was 7 of us on one pill because that was all family, yeah. We would cook it on the can, burn it on the bottom and then burn it on the top, and at that time sometimes we might have to put 300 units of water on it because there would be so many of us, and then that would be just enough for each of us to get 40 units or something, and then one person would work it in with the cotton in it, draw it up, and split it with everybody's needle. [Split it in] even amounts, like 30–40 units in each needle.
d. Overall injection episodefrequency	
Multiple injection episodes per day that include MIs per injection episode	Male, 22 years old: You can get 2 or 3 shots off a quarter [Opana ER] … I do Opanas at least 15 to 20 times [total] a day. That's, at least, at least 4 or 5 quarter pieces a day. Female, 37 years old: I would probably inject about 10 times a day. When you're sharing you want to inject more because when they're not in my house I inject probably 4 times a day because I'm getting that whole quarter to myself. Male, 43 years old: Me and the lady [syringe exchange program counselor] had a miscommunication. She was like, 'how many time do you do a pill a day?' And, I was like 'well, 5 or 6'. She was thinking 5 or 6 times I'd stick myself. And, see she didn't ask me how many times I stick myself. She asked me how many pills

Key Themes	Exemplar Quotes
	I do a day. And, so that worked out a lot different when she figured [multiple injections per injection episode], you know, ok 5 times 7 is 35 rigs. You know, 35 needles.

[a] Multiple injections per injection episode refers to a practice that occurs when the volume of the drug solution prepared from a single dose of the drug is larger than the volume of the available syringe. Thus, each time a drug solution is prepared for injection (i.e., injection episode), multiple injections are needed to administer the volume prepared. All participants in this study reported using 1 mL insulin syringes with fixed needles.

[b] All participants were aware of the HIV outbreak in this community at the time of the interview. During the interview, participants were asked to describe experiences before they became aware of the outbreak and after. All quotes in this table represent participants' typical injection experiences, which were the same before and after becoming aware of the HIV outbreak except when noted by "[before the HIV outbreak]" in the quote.

[c] OPANA® ER with INTAC®, a proprietary formulation of extended-release oxymorphone with non-FDA approved abuse deterrent formulation.

[d] OPANA® IR, instant-release oxymorphone.

[e] Backloading is a syringe-mediated drug sharing practice when one-piece, 1 mL syringes are used. The plunger is taken out of the receiving syringe to expose the back-opening of the syringe, and the needle of the donor syringe is inserted into the back opening to transfer the drug solution.