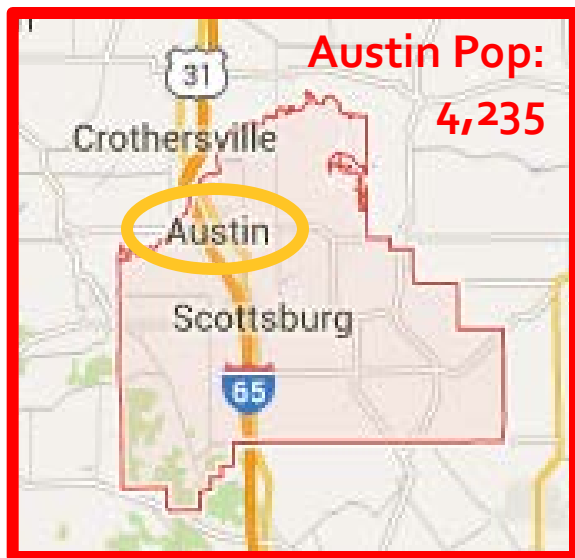


The Illicit Injection of Prescription Opioids in Scott County, Indiana: Risks and Rewards

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- Population: 24,000 (Austin : 4,235)
- High poverty (19.0%)
- High unemployment (8.9%)
- Low educational attainment (21.3% have not completed high school)
- Ranked last among 92 counties in a variety of health and social indicators, including life expectancy



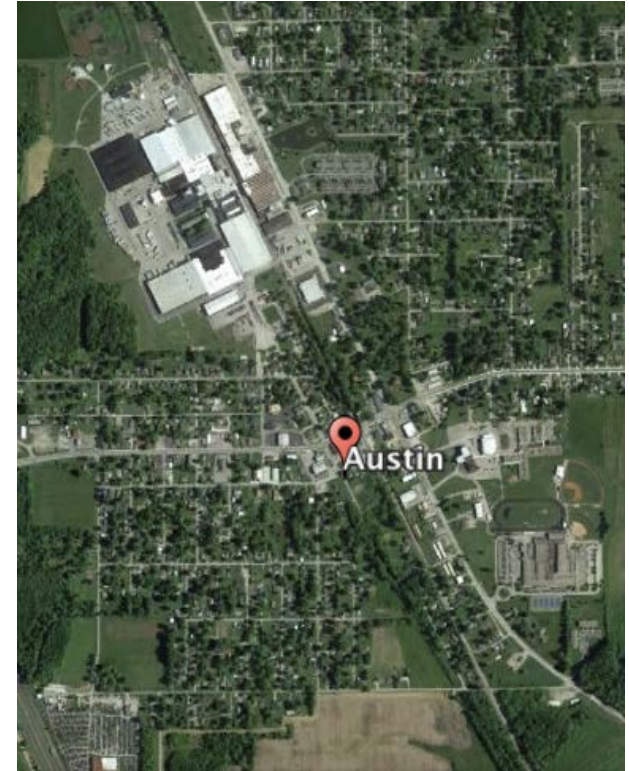
Specific Aim of Qualitative Investigation

- ❖ **To investigate behavioral and structural risk factors that contributed to the rapid dissemination of HIV infection among a community of PWID in Scott County, Indiana.**

Qualitative Methods

❖ Eligibility criteria

- 18 years of age or older
- Resident of Scott County
- Able to complete interview in English
- Injected drugs in the past 12 months
- Able to provide informed consent



Qualitative Methods

➤ Sampling

- Convenience/Purposive
- Syringe service program (SSP), street recruitment, peer recruitment

➤ Interview setting

- Local church and SSP
- Increased need to ensure privacy



Austin, Indiana









❖ **Data Collection: June-September, 2015**

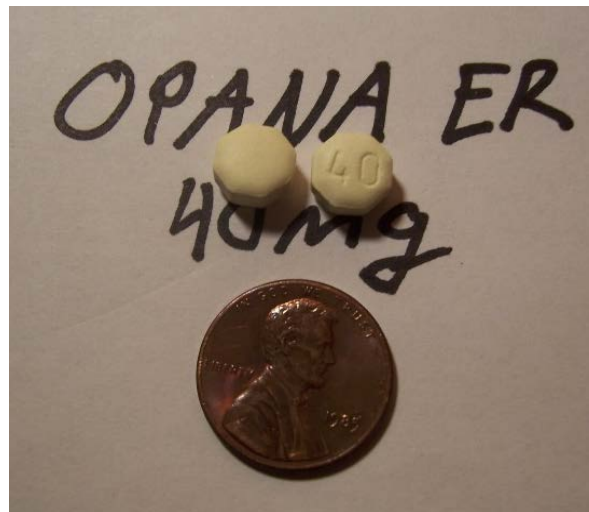
- 4 focus groups (31 individuals)
- 25 private interviews (25 individuals)
- Audio-recorded and interview notes
- No identifying information collected

Characteristics of Persons Interviewed (N=25)

Age (median, range)	33 years (19-57)
Non-Hispanic White	25 (100%)
Female	11 (44%)
Austin, IN residence	21 (84%)
Primary drug injected	
Opana ER	22 (88%)
Opana IR	1 (4%)
Methamphetamine	2 (8%)
Enrolled in SEP	19 (76%)
HIV-positive (self-report)	10 (40%)
HCV-positive (self-report)	21 (84%)

OPANA® ER (Oxymorphone Extended Release)

Dosage Strength	OPANA® ER with INTAC® Tablet Images*	GENERIC oxymorphone ER Global Pharma (Impax) Tablet Images*
40 mg		
30 mg		



Brief History of Opana ER

- Oxymorphone is a semi-synthetic opioid analgesic
- Effect onset: 5 to 10 minutes; Effect duration: 3 to 4 hours
- Opana ER first approved in 2006 to treat moderate to severe pain
- Crush-resistant extended-release formulation with INTAC created in 2012
 - FDA did not approve abuse-deterrent labeling
- March 2017: FDA advisory committee determined that the benefits of Opana ER do not outweigh the risk
- June 2017: FDA requested that Endo Pharmaceuticals remove reformulated Opana ER from the market

Key Finding: Frequent Injection Episodes with Multiple Injections

- ❖ **Most participants who inject OPANA® ER reported performing multiple injections per injection episode (MIPIE)**
 - Up to 7 injection episodes per day
 - 2-5 injections per injection episode
 - Typically shared a quarter of a pill with 2-4 injection partners
- ❖ **MIPIE** 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 1ml insulin syringes with fixed needles
- ❖ **MIPIE reported as common among PWID in the community**

Key Finding: PWID “Browned” OPANA® ER for Injection

- **INTAC®, a proprietary high-molecular-weight polyethylene oxide, added to OPANA®ER during reformulation in 2012**
 - Deterrent to prevent crushing, which is a requirement to insufflate and inject pills
 - PWID in Scott County applied moderate heat to “brown” OPANA® ER tablets to facilitate tablet dissolution in water

Polyethylene Oxide (PEO)

Guardian™ Technology Confers Physical and Chemical Barriers to Abuse



**Physical
(hardness)**

Injection molding machine

Well-characterized process,
differentiated by heat & pressure

**Chemical
(polymer matrix)**

Polyethylene oxide (PEO)

Viscous hydrogel on
contact with liquid

**Extended-release profile with
physical and chemical
abuse-deterrent properties**

“Browning” the Pill

I cut it [Opana ER] 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.

(White male, 34 years)

"Browning" the Pill



Hydroxy Ethyl Cellulose (HEC)

➤ Extended Release formulation uses HEC as time release mechanism

- Forms viscous gel in aqueous environment *in vivo* that slowly releases drug through diffusion and erosion during gastrointestinal transit
- Similar process occurs *ex vivo* when HEC encounters water in drug cooker
- PWID add additional water to the crushed pill to oversaturate cellulose to generate a more watery mixture capable of being drawn into a syringe

Specification	
	
Hydroxy Ethyl Cellulose (HEC)	
ITEM	Value
Molar Substitution Degree	1.8-3.0
PH value(1%, .sol.)	5.5-8.5
Water insoluble (%)	1.5 Max
Ash (%)	5.5 Max
Particle size (% , 60mesh)	98 Min
Moisture (%)	5.0 Max
Viscosity (mpa·s)	300-100,000
HEC Hydroxy Ethyl Cellulose	

Multiple Injections per Injection Episode

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. For 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... 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.

(White male, 43 years)

Multiple Injections per Injection Episode

“I get a quarter of a pill and I cook it. And when I work the pill up, I'd put like 120 units of water on it, which would give [the four of] us like 30 units apiece. We'd have 1 syringe; I'd do a shot, rinse it out, let them draw theirs up and do a shot, rinse it out, and then do it again.”

(White Male, 33 years)

KEY FINDING: “Rinse Shots”

PWID “rinsed” the cooker by adding extra water after the original solution was injected to ensure all drug was extracted from residue. This is referred to as *a rinse shot*.

“I get one [shot] off of it then give it away to somebody that needs it or wants it...like me and my husband we'll split the 100 units...we'll just give somebody else the can and be like, “Here, you can have it...Cause you know there's a rinse.” (White Female, 27 years)

Infectious Disease Risk Associated with MIPiE

[Before the HIV outbreak] I'd go and 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. (White Female, 40 years)

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. (White Female, 37 years)

“Rinse Shots” are uncommon with other drugs injected

[With heroin, you inject] one time and you're good, you know. If you've got decent dope [heroin], you do a shot and you're good, you know. I've seen people try to take, get three or four shots off of it [heroin], but you can't, you know, because with heroin it's one shot and you're done.

(White Male, 33 years)

“I literally place it [Opana IR] in the cooker and put water on it. I then stir it and draw it up with no heat.”

(White Male, 19 years)

High Cost of Opana Influences Disease and Overdose Risk

Increasing price of diverted drug created pressure to inject together:

“Well, if you buy these pills, a whole pill is like 200 dollars. And sometimes we'd have just enough [money] to get high for a quarter of one [pill]. Sometimes 2 or 3 of us would do a quarter of a pill.”

“There are sometimes we inject with another person...And it's usually to help us because we can't make enough money to get that quarter [pill], and it's usually like the first quarter of the day because I'm sick, 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.”

High-Risk Injection Networks

No one even thought about HIV and then all it took was just one [positive] person to come into the group. There'd be 5 people in that group that share with that one person. Each of those shared with each other anyways. And then 1 of the 5 people went to other groups. (White Male, 43 years)

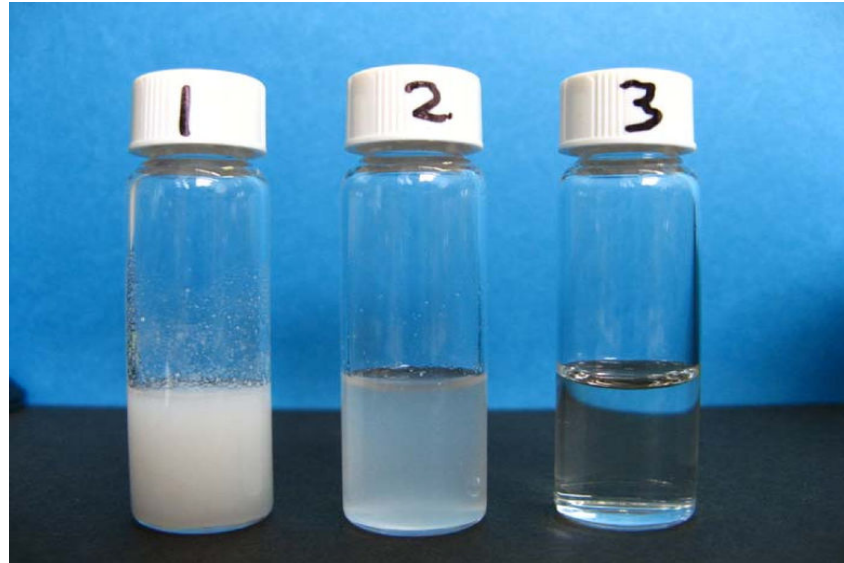
There could be different people using different houses. It doesn't matter what house. It's not that you would go to the same house all the time. You would just go to whatever house was available. (White Male, 39 years)

MIPIE's influence on Harm Reduction Practice

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 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.

[White Male, 43 years]

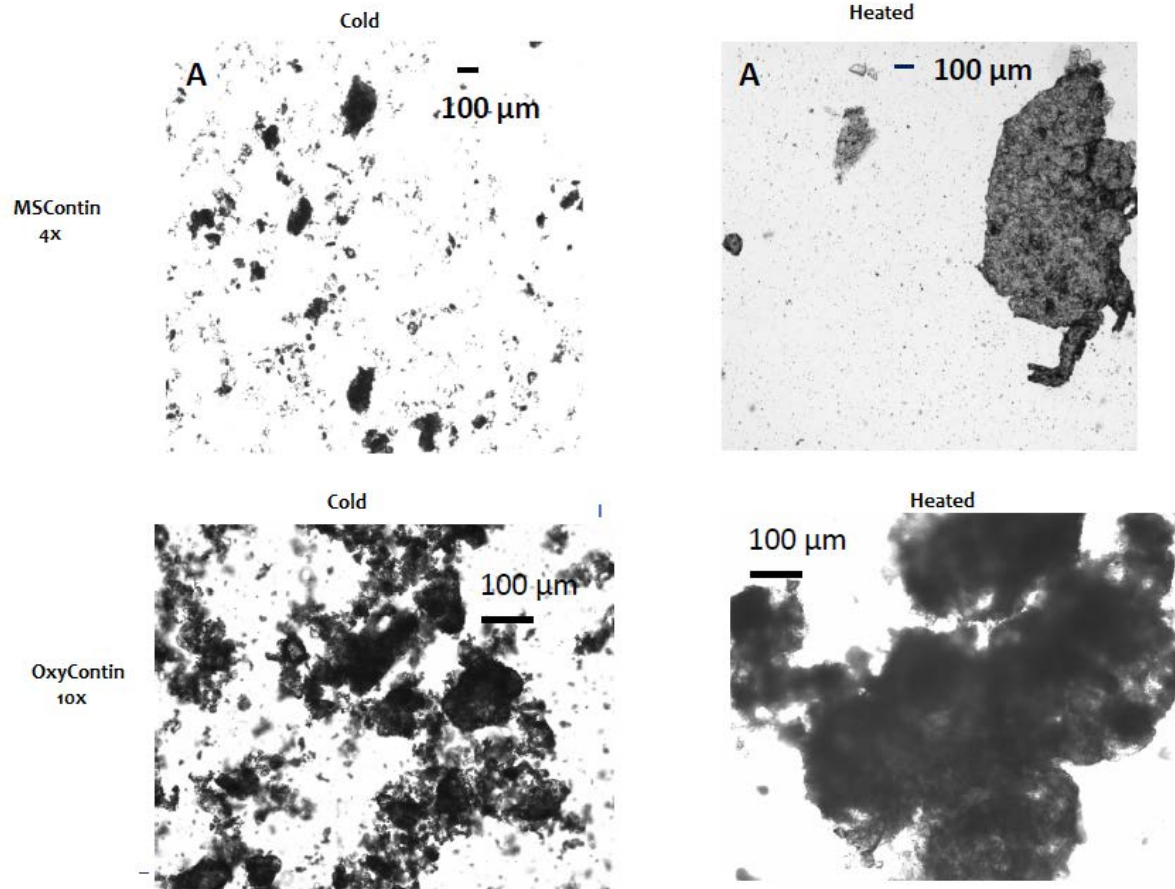
Dangers Associated with Lack of Filtration



Injection Mixtures (cold extraction)

1. Unfiltered
2. Cigarette filtrate
3. Cigarette then 0.45 μ m

Unfiltered Pill-based Solution Under Microscope



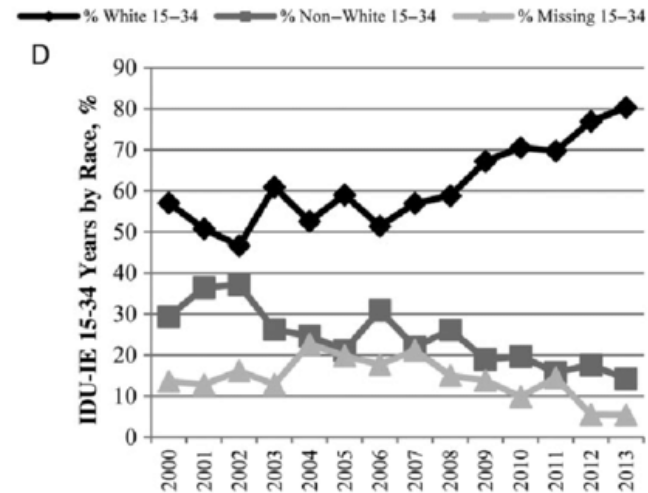
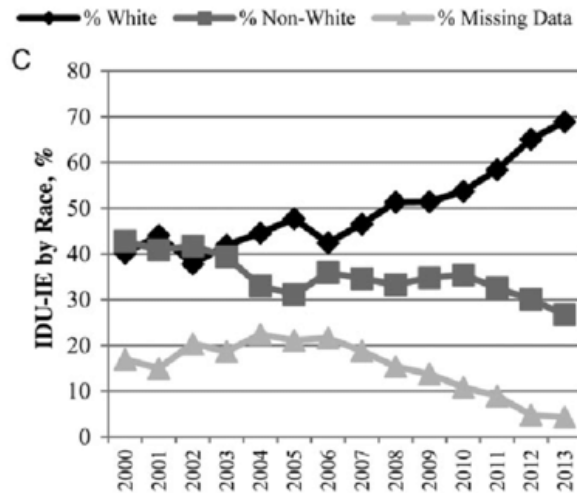
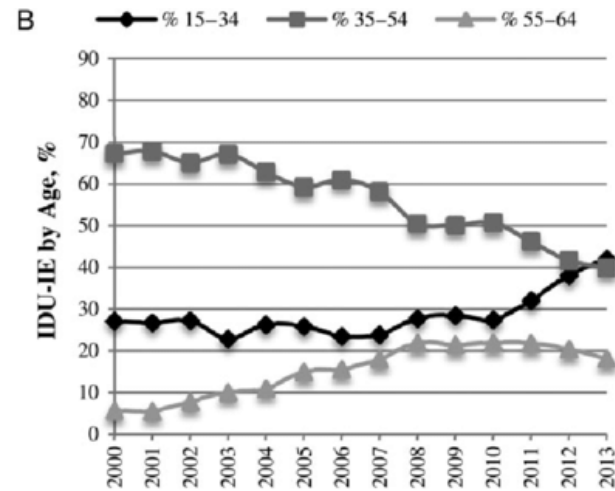
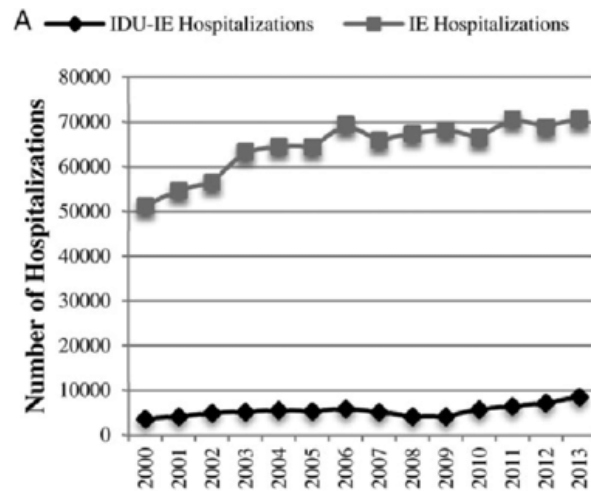
Wheel Filters, 30mm/0.22 μ m



Unfiltered vs. Filtered Aqueous Solutions of Oxycontin and Subutex



Increasing Infectious Endocarditis Admissions Among Young PWID



Conclusions

- Circumventing anti-crush mechanism (INTAC)
- Circumventing Gelling Associated with ER Excipients
- Rinse shots
- Economics of supply and demand
 - Increase HIV and HCV risk
 - Decreases OD risk
- “House Hopping”
- Filtration: Endocarditis and Pulmonary Embolism
- From Opana to Heroin and Illicitly-made fentanyl
 - Increased overdose risk
- MIPIE associated with other extended-release opioid formulation (e.g., oxycodone ER; hydromorphone ER)
- TTP-like effects reported in Tennessee

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