

Answered and Unanswered Questions about Counterfeit Drugs

Targeted Literature Review

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Goal of Presentation

- Substantial concern for adulterated products in the recreational drug supply, particularly fentanyl
- What is known (and not known) about use, prevalence, and identification of counterfeit drugs?
- Examined literature for 5 foundational questions about recreational counterfeit drugs
 - Implications for surveillance
 - If you are doing research in this area and I don't highlight it, please connect with me!

Q1: How are counterfeits defined?

World Health Organization¹

“Falsified medical products”: Medical products that deliberately/fraudulently misrepresent their identity, composition or source

Drugs sold illicitly by unlicensed individuals (in person or online)

- Number of active chemicals detected via chemical analysis
- Comparison of composition to look

Fraudulent pharmaceuticals sold in unlicensed online pharmacies

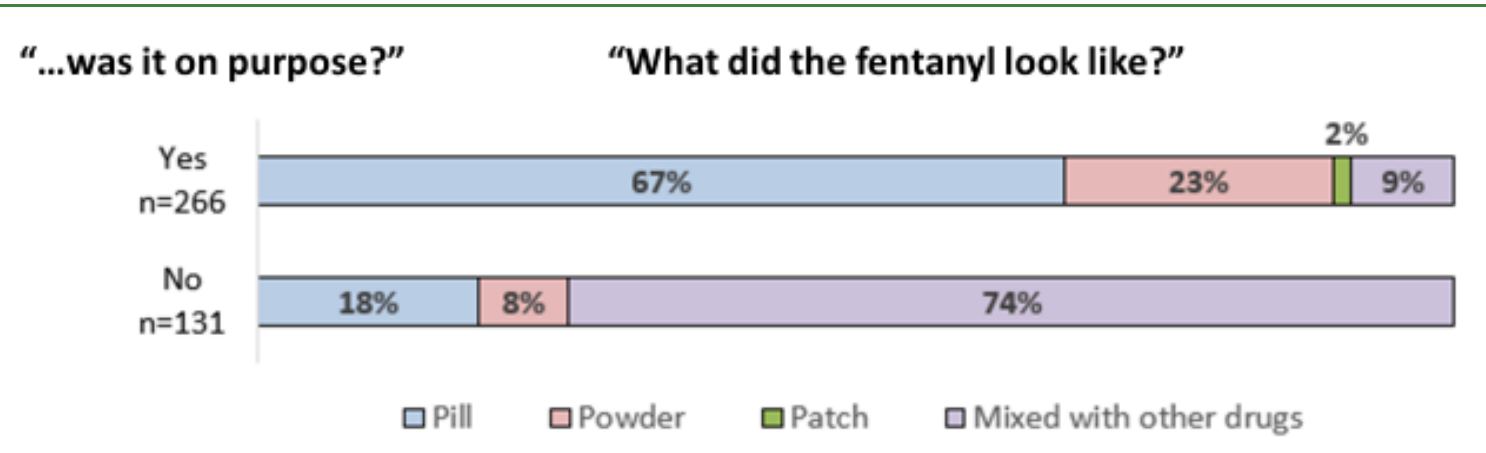
- Important area of research
- Direct composition studies not conducted

Fraudulent pharmaceuticals sold in licensed pharmacies

- Concern in low- & middle-income countries
- Drug does not contain full or expected amount of drug

Q2: What attitude(s) do PWUD have toward counterfeits?

2021 Study² of people who use drugs (PWUD) and utilize a syringe exchange program in Washington showed that 42% of respondents had used fentanyl in the past 3 months; among those, 67% used fentanyl intentionally.

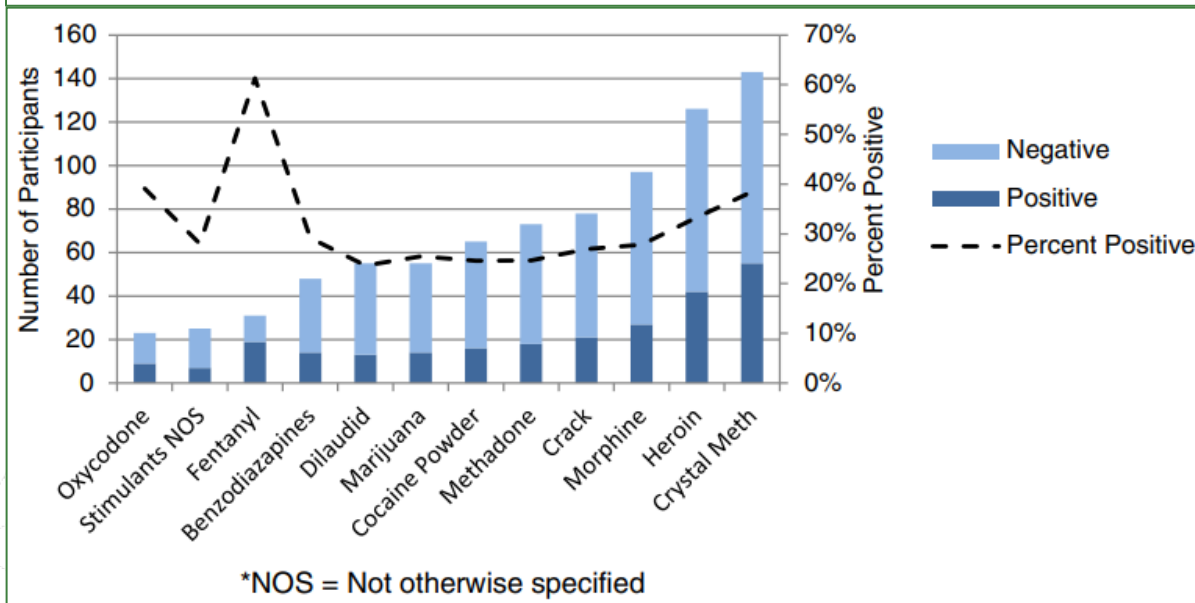


Q2: What attitude(s) do PWUD have toward counterfeits?

However, those who are exposed to fentanyl might not know it.

From among PWUD at harm reduction sites in British Columbia in 2015³, 29% tested positive in urine screen for fentanyl; among those, only 27% reported knowingly using fentanyl in the past 3 days.

Among 5 reporting overdose in the past week, all tested positive for fentanyl, 2 unknowingly.



Knowledge gaps:

- True (unbiased) exposure challenging to know in any given study
- Changing perceptions from 2015 to 2022?
- Would PWUD seek fraudulent pills over other forms?
- Does emulation of pharmaceutical translate to perception of safety among PWUD?

Q3: How do PWUD identify counterfeits?

2021 literature review of mobile apps⁴, most from Apple's and Google's app stores. Apps claimed to detect via imprint, color, or shape. Few via photograph or bar code. App assessment lacked direct evaluation of accuracy; user perception is the only standard.

2020 street interview study⁵ in Baltimore indicated PWUD can be empowered by test strips by promoting market transparency, but people were wary of constantly changing market conditions.

Knowledge gaps:

- How do tools, such as apps and test strips, compare to a personal network of trust (e.g., an impersonal dealer vs a friend vs an app)?
- Uptake of different technologies by PWUD? How many unique users of each technology are there and are groups being missed?
- How agile can technologies be in changing market conditions, such as emerging drug combinations?

Q4: What is the size of the market for counterfeits?

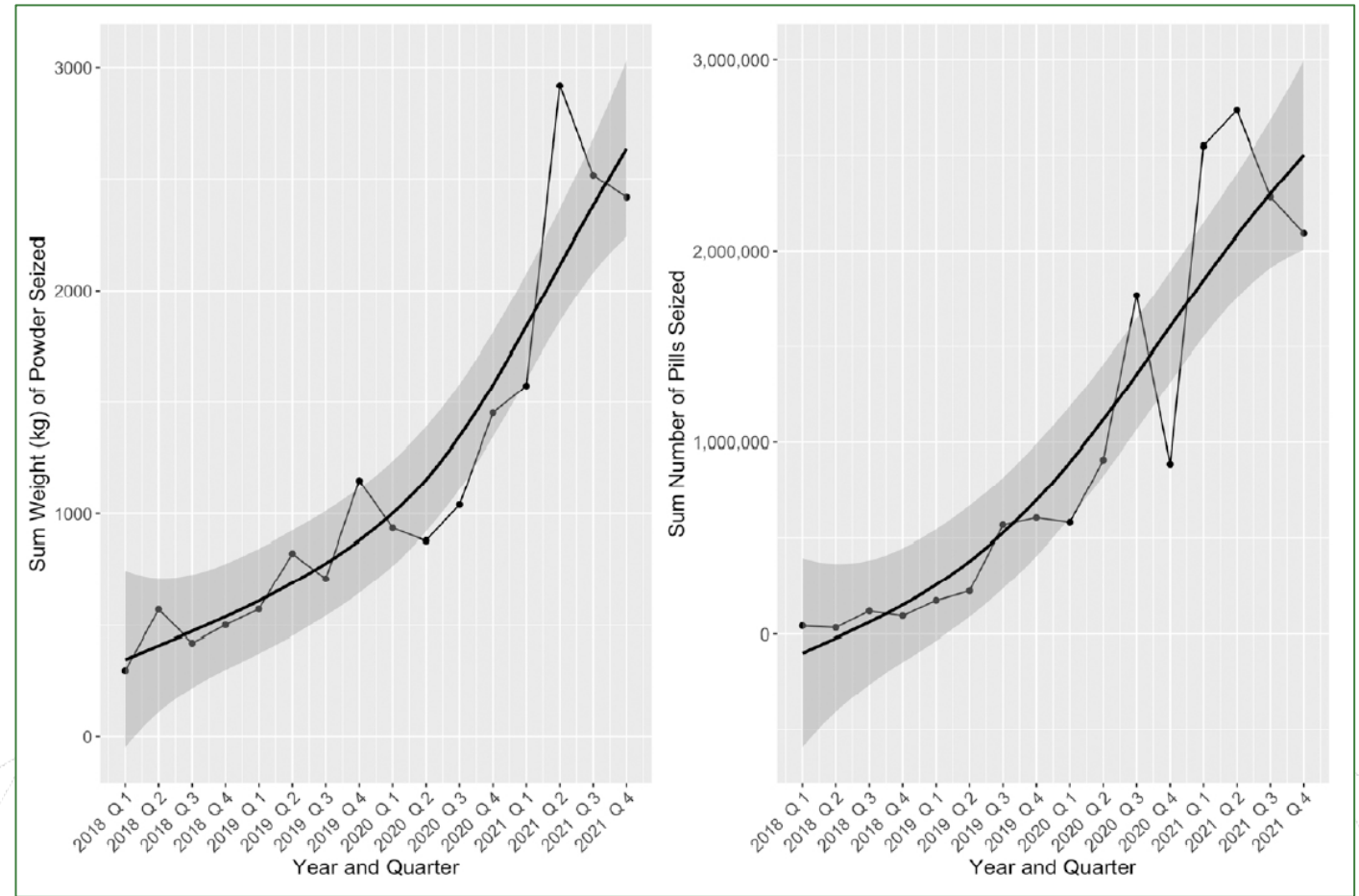
The market for fentanyl is only going up.

Assessment of seizures over the past 4 years shows ever increasing amount of drug, both in powder and in pill forms.⁶

Pill seizures grew from near zero in 2018 to over 2M pills in 2021; pills constituted >25% of seizures in 2021.

Knowledge gaps:

- True market may be impossible to know
- How does market growth translate to changes in exposure for PWUD? Are the same individuals exposed more often, more individuals exposed, or both?



Q5: What drugs are being emulated?

Case reports show fentanyl emulation of:

- Alprazolam in 2016⁷
- Hydrocodone/Acetaminophen in 2016⁸
- Hydrocodone in 2017⁹
- Oxycodone in pediatric patients in 2021¹⁰

Pills from patients at UCD show emulation not involving primarily fentanyl^a

Knowledge gaps:

- How and why are pharmaceuticals selected as candidates for emulation?
- What level of skepticism or risk perception (if any) do PWUD have toward “pharmaceuticals” purchased on the street?
- Beyond fentanyl



Concentration	Yellow Pill	Green Pill
Major	Etizolam	Etizolam
Possibly Moderate	Cocaine	Cocaine
		Ketamine
		Methamphetamine
Trace-Minor	Clonazepam	Clonazepam
	Ketamine	Flualprazolam
	Lidocaine	Lidocaine
	Methamphetamine	MDMA
	MDMA	Oxycodone
	Oxycodone	Fentanyl
	Fentanyl	Furanylfentanyl

Implications for Drug Surveillance

- Counterfeit drugs should be separately identified in data sources, when possible
- Potential to misclassify exposures or outcomes
- Confounding in estimates of effects a substantial issue
 - Ex: Difference in cocaine overdose trends with and without fentanyl¹¹
- Need to assess risks from online pharmacies¹², as one study indicated a third of pharmacy-related internet traffic is directed to illicit online pharmacies, rather than legitimate pharmacies¹³

References

Q1 – How are counterfeits defined?

1. A study on the public health and socioeconomic impact of substandard and falsified medical products. Geneva: World Health Organization; 2017. License: CC BY-NC-SA 3.0 IGO.

Q2 – What attitudes to PWUD have toward countefeits?

2. Kingston S, Newman A, Banta-Green C, Glick S. Results from the 2021 WA State Syringe Service Program Health Survey. Seattle, WA: Addictions, Drug & Alcohol Institute, Department of Psychiatry & Behavioral Sciences, University of Washington, March 2022.
<https://adai.uw.edu/syringe-survey-2021>.
3. Amlani A, McKee G, Khamis N, Raghukumar G, Tsang E, Buxton JA. Why the FUSS (Fentanyl Urine Screen Study)? A cross-sectional survey to characterize an emerging threat to people who use drugs in British Columbia, Canada. Harm Reduct J. 2015 Nov 14;12:54. doi: 10.1186/s12954-015-0088-4. PMID: 26577516; PMCID: PMC4650899.

References

Q3 – How do PWUD identify counterfeits?

4. Ciapponi A, Donato M, Gülmezoglu AM, Alconada T, Bardach A. Mobile apps for detecting falsified and substandard drugs: A systematic review. PLoS One. 2021 Feb 4;16(2):e0246061. doi: 10.1371/journal.pone.0246061. PMID: 33539433; PMCID: PMC7861418.
5. Weicker NP, Owczarzak J, Urquhart G, Park JN, Rouhani S, Ling R, Morris M, Sherman SG. Agency in the fentanyl era: Exploring the utility of fentanyl test strips in an opaque drug market. Int J Drug Policy. 2020 Oct;84:102900. doi: 10.1016/j.drugpo.2020.102900. Epub 2020 Aug 5. PMID: 32769054.

Q4 – What is the size of the market for counterfeits?

6. Palamar JJ, Ciccarone D, Rutherford C, Keyes KM, Carr TH, Cottler LB. Trends in seizures of powders and pills containing illicit fentanyl in the United States, 2018 through 2021. Drug Alcohol Depend. 2022 May 1;234:109398. doi: 10.1016/j.drugalcdep.2022.109398. Epub 2022 Mar 31. PMID: 35370014; PMCID: PMC9027012.

References

Q5 – What drugs are being emulated?

7. Arens AM, van Wijk XM, Vo KT, Lynch KL, Wu AH, Smollin CG. Adverse Effects From Counterfeit Alprazolam Tablets. *JAMA Intern Med.* 2016 Oct 1;176(10):1554-1555. doi: 10.1001/jamainternmed.2016.4306. PMID: 27532131.
8. Sutter ME, Gerona RR, Davis MT, Roche BM, Colby DK, Chenoweth JA, Adams AJ, Owen KP, Ford JB, Black HB, Albertson TE. Fatal Fentanyl: One Pill Can Kill. *Acad Emerg Med.* 2017 Jan;24(1):106-113. doi: 10.1111/acem.13034. Epub 2016 Oct 31. PMID: 27322591.
9. Armenian P, Olson A, Anaya A, Kurtz A, Ruegner R, Gerona RR. Fentanyl and a Novel Synthetic Opioid U-47700 Masquerading as Street "Norco" in Central California: A Case Report. *Ann Emerg Med.* 2017 Jan;69(1):87-90. doi: 10.1016/j.annemergmed.2016.06.014. Epub 2016 Jul 26. PMID: 27473610.
10. Joynt PY, Wang GS. Fentanyl contaminated "M30" pill overdoses in pediatric patients. *Am J Emerg Med.* 2021 Dec;50:811.e3-811.e4. doi: 10.1016/j.ajem.2021.05.035. Epub 2021 May 15. PMID: 34030905.

References

Implications for Drug Surveillance

11. Mattson CL, Tanz LJ, Quinn K, Kariisa M, Patel P, Davis NL. Trends and Geographic Patterns in Drug and Synthetic Opioid Overdose Deaths - United States, 2013-2019. *MMWR Morb Mortal Wkly Rep.* 2021 Feb 12;70(6):202-207. doi: 10.15585/mmwr.mm7006a4. PMID: 33571180; PMCID: PMC7877587.
12. Clark F. Rise in online pharmacies sees counterfeit drugs go global. *Lancet.* 2015 Oct 3;386(10001):1327-8. doi: 10.1016/S0140-6736(15)00394-3. PMID: 26460765.
13. Zhao H, Muthupandi S, Kumara S. Managing Illicit Online Pharmacies: Web Analytics and Predictive Models Study. *J Med Internet Res.* 2020 Aug 25;22(8):e17239. doi: 10.2196/17239. PMID: 32840485; PMCID: PMC7479587.

Thank you!
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