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A Field Study of the Opioid Market: Authenticity and Price from Pharmacy to Street

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American Enterprise Institute

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Roger Bate

October 2018

Abstract

With the assistance of pain patients, the opioids oxycodone and hydrocodone were assessed from licit and illicit sources in Philadelphia and surrounding counties. Sources included brick-and-mortar pharmacies, web pharmacies operating illegally by selling products without prescriptions, other internet sources such as social media fora, and private dealers. Pricing information was collected, and products were authenticated using Raman spectroscopy. All the legally obtained products were cheap and authentic, the web pharmacy and other internet products procured without prescription were more expensive, and a few were not authentic. Privately procured or assessed products were far more expensive, and over 15 percent were not authentic. If replicated in larger and better stratified studies, this result could indicate some problems for individual health and current policy if pain patients are driven from legal to illegal markets.

Two of the most popular opioids available on both the licit and illicit market are oxycodone and hydrocodone (Elder 2017). They come in a variety of formulations and dosages and together accounted for over 820m prescriptions dispensed between 2010 and 2014 (RADARS 2017).

This study aims to assess whether the versions of these medicines people actually buy are authentic and how much they pay for them. With the assistance of numerous pain patients who regularly use opioids several types of assessment were undertaken. The first were legal purchases with prescriptions at brick-and-mortar pharmacies. The second were purchases from web pharmacies that do not demand prescriptions. The third were either purchases, or scans without purchase, of internet-sourced products. (Some were scanned in a face-to-face meeting following a social media interaction, and others followed purchase via internet similarly to web pharmacy purchases.) The fourth were purchases or assessments from the street or via personal networks. This included actual purchases from dealers and, where possible, the screening of a dealer's relevant products over time (recording the sales price that will be charged).¹ This final approach is by far the cheapest and provides the largest sample size.

The study was undertaken in Philadelphia and the suburbs and peri-urban areas of Philadelphia. Internet purchases were sourced from numerous and often unknown locations.

Known versions of available medicines were scanned with a Raman spectrometer, and the resulting scan was used as a reference standard to compare collected samples. The spectrometer cannot determine what substances are present in a given sample, but rather measures how close the sample compares to the known reference standard measured by a P value. This type of spectrometer has been used for this type of drug quality assessments before and is also widely used by the pharmaceutical industry to ensure quality control of medicines and precursor chemicals (Bate and Hess 2010; Bate et al. 2013). Resulting P values were then plotted alongside pricing information and compared across procurement methods.

Demand for Opioids

The demand for opioids has grown rapidly over the past three decades in the US—both in the licit and illicit markets. According to a recent report from IQVIA, per capita opioid usage increased from a mere 134 milligrams morphine equivalent (MME) per adult in 1992 to a peak of 1,011 MME per adult in 2011 (IQVIA 2018). Although total opioid consumption has fallen to 599.3 MME per capita in 2016—accompanying a 15 percent reduction in opioid prescriptions—the figure is still considered high by the Centers for Disease Control and Prevention (CDC) (CDC 2017).

While numerous patients have legitimate pain needs, the increase in prescribing that occurred in the 2000s left many patients with an abundance of pills that were easily diverted into illicit markets or in some cases misused by the patients themselves (CBHSQ 2017). Since 1992 the number of American adults seeking treatment for addiction to prescription opioids increased by a staggering ninefold (CBHSQ 2016; CBHSQ 2017b).

As the number of Americans addicted to opioids increased, so too have overdoses. According to the CDC, there were 42,249 fatal overdoses in 2016 involving an opioid, and approximately 35 percent

¹ Competition obviously means buyers have a choice and can reject a seller's price, but from the evidence gathered in this paper, the vast majority of the time dealers receive the price they demand.

of those overdoses involved a prescription opioid, such as oxycodone or hydrocodone, alongside potentially many other substances. The death toll from opioid overdoses is unprecedented with the overdose rate from opioids now nine times that during the peak of the heroin epidemic in the 1970s (National Center for Health Statistics).

Limiting the Supply of Opioids

In recent years the legal opioid supply has shrunk following measures taken by both the federal government and several state governments. Several state laws now limit the duration of opioid prescriptions for acute pain, and in 2016 the CDC released guidelines encouraging physicians to prescribe “the lowest effective dose,” which subsequently have been responsible for a dramatic reduction in prescriptions (Dowell et al. 2016; NCSL 2018). While these policies have certainly aided in reducing the supply of opioids (Chiu et al. 2018), such reduction has come at a price.

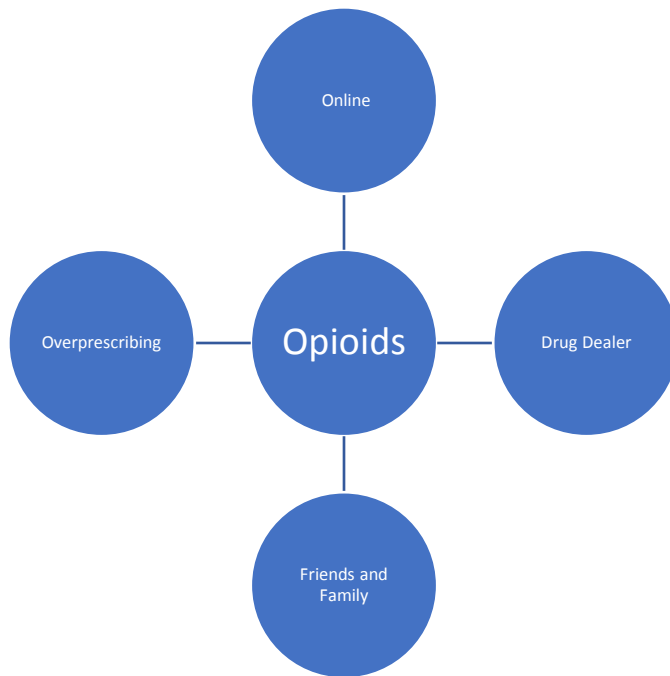
Demand for opioids—by those addicted and others that might have experienced a rapid dose reduction and are now in “need” of pain medication—may have switched from the legal market with prescriptions, physician oversight, and quality control to one of illicit trade, organized crime, and no health oversight. There is certainly evidence that the market for heroin has changed with older first-time users, who first were hooked on prescription drugs (Cicero et al. 2014).² Most patients who would swallow pills will likely not snort or inject substances of unknown provenance (at least until addiction takes control), but illicit markets contain millions of seemingly legitimate pills. More time is needed to fully assess opioid policy changes, but as the illicit opioid market changes, information is needed regarding the difference in quality and price of this market.

Figure 1 describes the main sources of ill-advised opioid use (Stone 2018).³ At the core of this paper is a question that arises from this figure. As physician overprescribing has reduced, did demand just fall, or was it picked up by other sources? If so, what is the quality from those sources?

Figure 1. Ill-advised opioid use

² The authors assess that the “respondents who began using heroin in the 1960s were predominantly young men (82.8%; mean age, 16.5 years) whose first opioid of abuse was heroin (80%). However, more recent users were older (mean age, 22.9 years) men and women living in less urban areas (75.2%) who were introduced to opioids through prescription drugs (75.0%).”

³ There is a heated debate about what constitutes overprescribing. In the summer of 2018, there was increasing concerns that chronic pain patients may now be being under-prescribed.

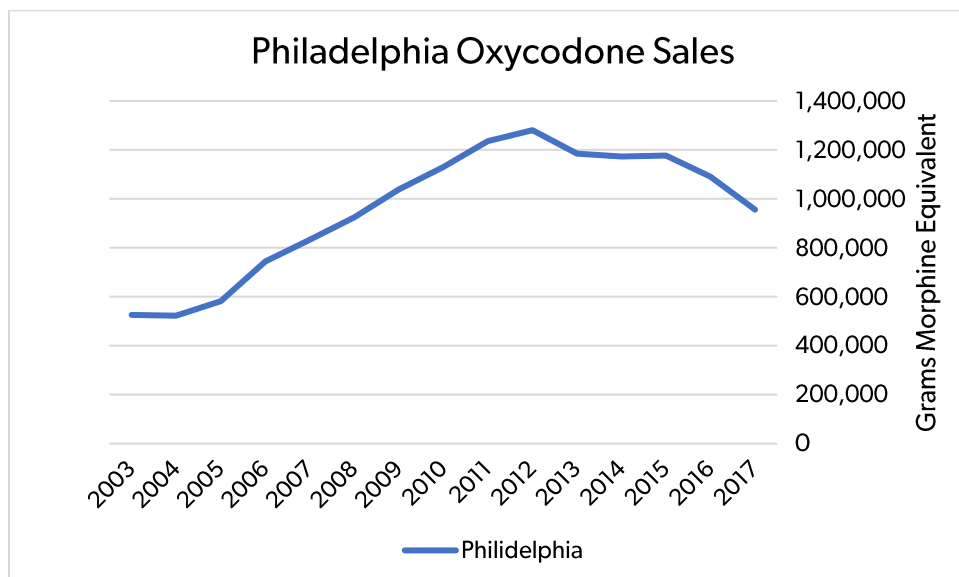


Source: Author

Setting

This study takes place in Philadelphia. This city and its suburban counties have been affected with opioids like so many others in the US. And like the rest of the US, sales of opioids in Philadelphia have followed a familiar pattern for oxycodone as shown in Figure 2.

Figure 2. Philadelphia Oxycodone Sales

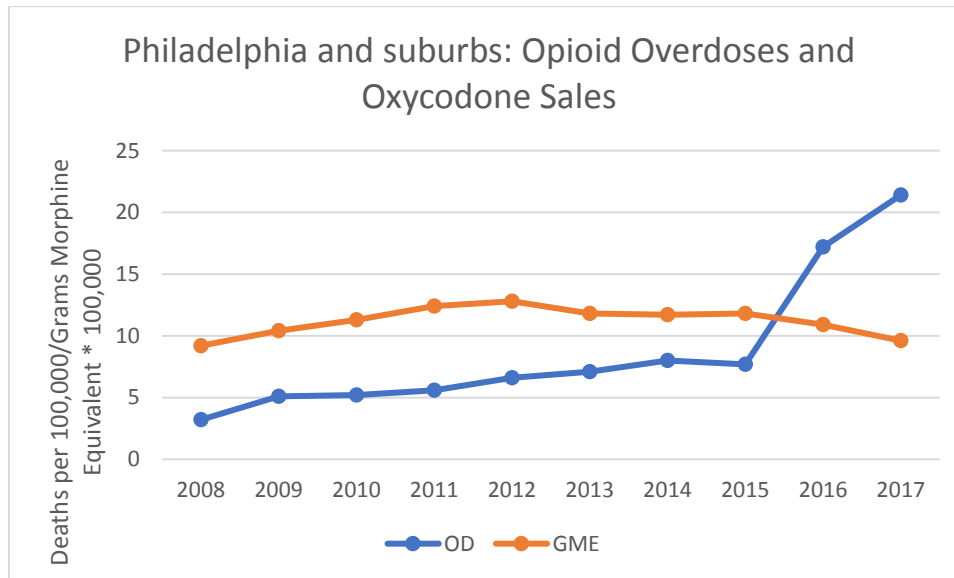


Source: DEA

Sales of legally acquired oxycodone (and other opioids) peaked a few years ago. But what is also true is that overdoses have increased in the recent past as legal opioid sales have fallen.

Figure 3 shows deaths from opioid overdoses in the city and counties relevant to the research undertaken in this paper and compared against legal opioid sales.

Figure 3. Philadelphia and Suburbs: Opioid Overdoses and Oxycodone Sales



Source: City of Philadelphia / DEA

The data for 2017 are estimated based on the city only since official data from the Philadelphia suburbs are not yet available.

As I have documented elsewhere (Bate 2018), anecdotally the overprescribing market is slowing, and the vast amounts dealers can make from it are falling too. In June 2018 one dealer could charge about \$18,000 per month for an outlay from patients of only \$500, increasing addiction and criminality far and wide. As supply dwindles, these addicts will buy products of dubious provenance from elsewhere.

Methods

For several months in 2018 I spent time talking with numerous pain patients, some of whom have been in drug treatment programs. They allowed me to assess the products they procured or even allowed me to assess products before they were procured. Samples of oxycodone and hydrocodone were obtained through the following three methods:

1. Purchase with prescription from legitimate brick-and-mortar pharmacies,

2. Purchase without prescription from internet pharmacies,⁴ and
3. Purchase or scanning of non-purchased products from private dealers.

Raman Spectroscopy

Raman spectrometers have frequently been used as a quick, reliable, and cost-effective way to differentiate between genuine and counterfeit drugs (Bate and Hess 2010). The device compares an unknown sample—in this case a pill—to a reference standard by comparing the frequencies of certain kinds of light that are scattered after the two substances have been illuminated with a monochromatic laser (Witkowski 2005). The resulting “spectra” from the scans are compared by the device, which generates a P value denoting the probability that the difference between the reference standard and the sample is due to measurement uncertainty rather than the difference in molecular structure. Therefore, a P value of greater than or equal to 0.05 would represent a pass result (i.e., any difference is due to measurement uncertainty), while a P value of less than 0.05 would represent a failed result (Thermo Scientific 2014; Bumbrah and Sharma 2016).

While Raman spectroscopy has the advantage of allowing for comparisons without damage to the substance in question, it requires that the reference standards are identical to the substances being tested. Therefore, a match requires that the substance contains not only the same active ingredient as the reference standard but also the same binding agents, colorings, and other excipients.

A non-match then does not necessarily imply that the medicine does not contain the active ingredient of the reference standard (for example a generic cannot be substituted for branded drug), nor does it confirm that the substance is fake (as the product could be legitimate and have degraded). Rather, it shows that the substance is not consistent with the reference standard and would not pass the quality control standards of the manufacturer. To obtain the specific molecular contents of a drug, high-performance liquid chromatography, mass spectrometry, or other advanced techniques would be required. However, such methods are impractical for a rapid screening approach.

Testing

⁴ Pharmacychecker.com, one of the key credentialing organizations, told me this: “We’re very sympathetic to people with legitimate prescriptions for controlled medications who are struggling to afford them, but we long ago made the decision to ban non-U.S. pharmacies from our program that sell prescription narcotics or any controlled drugs into the U.S. Generally, international online pharmacies seem to stay away from selling controlled drugs at all into the U.S. That way they avoid people who may be seeking to obtain addictive medicines with phony prescriptions and stave off potential enforcement problems from the U.S. Drug Enforcement Agency. U.S. online pharmacies could sell prescription narcotics but must meet the requirements of the Ryan Haight Online Pharmacy Consumer Protection Act of 2008. Most do not do so. The PharmacyChecker-verified U.S. pharmacies do not sell prescription opioids online.” And Tim Smith of the Canadian International Pharmacy Association, the other important credentialing group, says this: “CIPA members do not sell controlled substances, narcotics or pseudoephedrine products.”

Using a Thermofisher TruScan spectrometer, samples obtained from each source were compared to a known reference standard. Given that products can be tested without damaging them,⁵ non-procurement testing occurred where possible. Samples using this means of testing include physicians' samples, pharmacy and online stocks, and street dealer samples. The resulting P value of each comparison was then charted alongside its corresponding price.

Results from this analysis are shown in Figures 1 and 2. Items that were not procured but still tested were added to the relevant procured list but carry no corresponding price information—except for items tested from a dealer's stock, which include pricing information based on dealer expectations. Desk research (using the crowdsourcing drug-pricing website streetrx.com) showed that it was unusual for either of the two opioids procured to cost more than \$2 per mg. And no pain patients I spoke with ever pay above this price, so it acts as a de facto cutoff, with no products purchased above this price.

Summary Data

The most important outcome from this analysis is that all the legitimately procured opioids were of good quality, whereas a few of the products bought without prescription from internet pharmacies and even more of the products bought (or assessed dealer samples) on the street failed authentication. Seventeen samples from physicians' stores and pharmacy stocks were also scanned, and all were authentic. Since no price data are attached, they are not included in the analysis. However, they do add to the evidence that medicines provided through the legitimate supply chain are authentic.

Tables 1 and 2 contain the summary data.

Table 1. Oxycodone price and quality data

Oxycodone	Legal Pharmacy	Web Pharmacy	Other Web	Street	Dealer Stock
Price (\$/mg)	0.027	0.16	0.15	0.84	0.93
P Value	0.29	0.19	0.16	0.17	0.15
Authentication Failure	0	1 (4.3%)	1 (6%)	3 (13%)	7 (13%)

Source: Author

Table 2. Hydrocodone price and quality data

Hydrocodone	Legal Pharmacy	Web Pharmacy	Other Web	Street	Dealer Stock
Price (\$/mg)	0.24	0.41	0.44	0.92	0.94
P Value	0.23	0.18	0.16	0.16	0.15
Authentication Failure	0	1 (6%)	1 (8%)	2 (11%)	10 (19%)

Source: Author

⁵ While scanning the outside of the pill can be enough for most medicines, thick pill coatings mean that the pill must be cleaved so that the inside can be scanned. While simple enough, it means damaging the product; hence, the approach is no longer noninvasive.

Out of a total of 253 samples of oxycodone (136) and hydrocodone (117), 26 (10 percent) failed authentication (12 oxycodone and 14 hydrocodone). The data indicate that street products are both less authentic and more expensive. Of the 147 samples from the street (either procured or scanned from within dealer samples), 22 (15 percent) failed authentication. Legally prescribed oxycodone is far cheaper than its street equivalent (Figure 4). Seven samples were offered at over \$2 per mg and were not procured from the street. Twenty-three samples of oxycodone could not be evaluated because it was not possible to be sure what exact brand (and hence Raman spectrum) to compare them against.

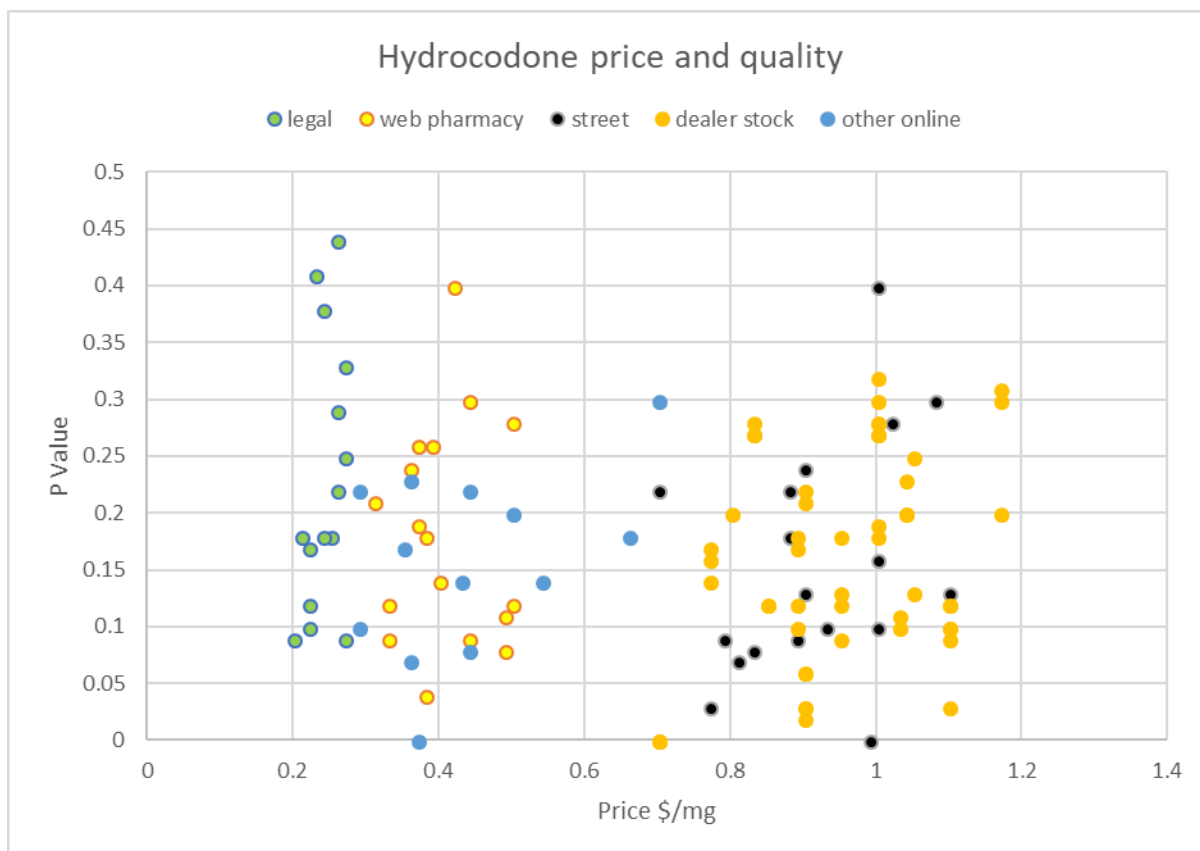
Figure 4. Oxycodone Price and Quality



Source: Author

The market for hydrocodone is similar, albeit the difference between legal and illegal price is smaller.

Figure 5. Hydrocodone Price and Quality



Source: Author

Legally prescribed hydrocodone is cheaper than its street equivalent, as Figure 5 shows. (Recall a P value of under 0.05 fails authentication.) Two samples were offered at over \$2 per mg and were not procured from the street.

Thirteen samples of hydrocodone could not be evaluated because it was not possible to be sure what exact brand (and hence Raman spectrum) to compare them against.

For both oxycodone and hydrocodone, averaging across all data, show that p values are lower at higher price, demonstrating an inverse relationship between quality and price.

Illicit Prices. One obvious caveat must be raised with price. Most prescriptions for legal products are for multiple pills (often 30), whereas street products are often for one or two pills. Bulk buying is always cheaper in nearly every product, so it is to be expected that street products would be more expensive. The history of prohibitions supports the notion that price is also likely to be higher in illegal markets.

Two of the pills bought on the street (one each for oxycodone and hydrocodone) appear to be counterfeit (zero P value), probably containing none of the correct active ingredient. Eleven of the dealer stock (five oxycodone and six hydrocodone) had zero P value and appeared counterfeit.

Thirty-five samples of dealer stock could not be properly tested because of thick coatings on the pills. To know the authenticity of the product would have required cleaving the pill to scan the inside, and since we did not procure these pills, that could not occur.

Discussion

The sample sizes for each category of purchase are relatively small, and a substantial number of samples (75) could not be tested either due to pill coatings or because of uncertainty about what to authenticate the samples against. As a result, any conclusions drawn from these data are speculative. While not testing is the correct protocol, some of the products are likely imports and hence illegal in some way, and with no obvious provenance, quality must be a concern. Not being able to infer anything from these samples may mean we are missing key data.

However, there seems to be a consistent finding across both drug types; namely, that several medicines bought illegally are not what they claim to be—either because of poor storage and subsequent degradation, substandard production, or counterfeiting. More detailed bench science would be required to ascertain exactly what they contained.

Illegal markets are often hard to measure for obvious reasons, but a related problem is that they are hard to model. The illegal “street” market encompasses everything from the tough corners as made famous in the HBO series *The Wire* to the apparently seemlier and definitely less dangerous trade that takes place in country clubs, gyms, bars, workplaces, and residencies. When describing street drugs in this paper, I am referring to this safer predominantly white middle-class arena.

It seems a fair assumption that the prices charged and the drug quality in such locations are respectively probably higher and better than on the more Hobbesian street. (Hence, this paper probably underestimates the risks from illegal supplies and may overestimate costs.) That does not mean the addiction and inherent danger of opioids to the real estate brokers, bankers, lawyers, and physicians that frequent such locations are not just as serious, just that they may be receiving different products (and far less likely to be offered heroin) than on actual street corners.

Additionally, on the street there are a vast array of products, such as pills, heroin (black tar, white powder, and brown powder), and other powders and potions that this paper has not even attempted to assess. It therefore reflects only a small part of the illicit drug market. Anecdotally, the few interactions with those at the riskier end of the market sell a larger array of products and many that would not be testable with the protocol in this paper.

Illegal markets are not blessed with overt quality control, and one could probably expect that supply would not be consistent across illegal suppliers or indeed over time. Of the 22 failures (out of 147 samples—15 percent) from street samples, six apparently came from one dealer alone. If one is exposed to his product, it will either be ineffective or potentially lethal depending on content. Of course if one avoided his products, the overall risk is lower. This finding has implications for sampling as much as it explains possible risks.

While a larger (and given the above more varied) sample size is required, these results have implications for both the public health community and policymakers attempting to respond to the opioid crisis. Substandard or counterfeit opioids pose a substantial risk to those misusing such substances (Partnership for Safe Medicines 2017). For example, if the medicine is either ineffective or contains a lower amount of opioid, it may lead an individual to take more of that product thinking the dose taken before was too low. Substandard products could also cause a user to substitute products, including heroin or fentanyl, in which quality is probably far more variable and potentially lethal even in

small doses (Whelan 2018).⁶ Moreover, counterfeit pills labeled as containing oxycodone or hydrocodone could contain unknown amounts of fentanyl, posing a substantial overdose risk.

As psychiatrist and AEI Scholar Sally Satel says of those receiving inferior medicine: “Users might respond by increasing the dose or just abandoning the drug altogether, recognizing that they got a bogus set of pills and using something even more dangerous. For some others, interestingly, the power of expectation can be so great, that they experience that same subjective effect anyway (Satel 2018).”

There were four samples (two oxycodone and two hydrocodone) bought from web pharmacies and other social media (illegally selling without prescription) that also were inferior in some way. This perhaps poses a great threat, because there must be thousands of individuals who would never dream of buying something from the street (at least until hopelessly addicted) but who would use a web pharmacy (even one breaking regulations) thinking it was likely to sell legitimate products.

All in all, the worse performance of illegal products might make the outcome of policies designed to limit opioid misuse suboptimal. Recent policy interventions limiting access to opioids has unfortunately driven many legitimate pain patients to turn to illicit markets for relief. Purchases made in these markets are not only illegal but also observed to be more expensive, less reliable, and potentially dangerous.

TruScan has obvious limitations. But new handheld technologies are becoming available to assess far more data from samples, such as fentanyl content. The aim is to expand the current study in this direction in the coming months.

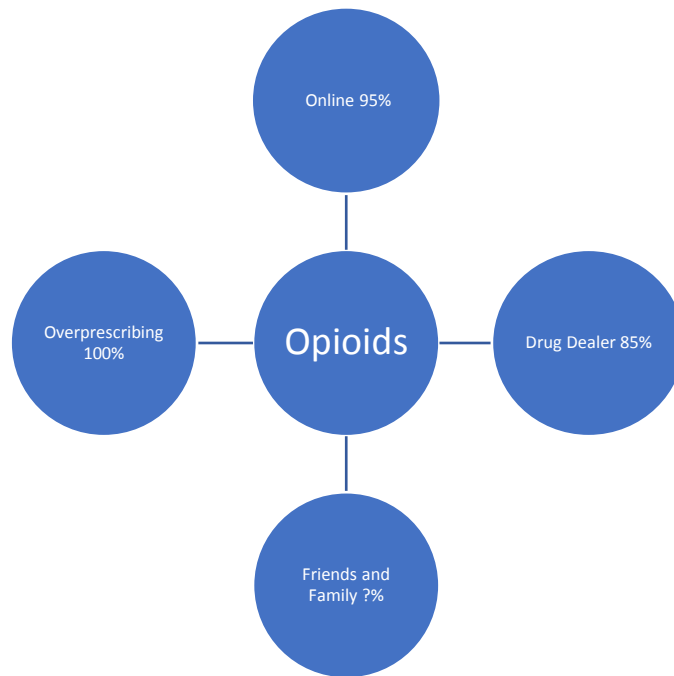
Conclusion

Opioids procured by pain patients from legal pharmacies, illicit web pharmacies breaking regulations, and private dealers were assessed for price and quality. The vast majority of opioids sampled were authentic, and all those obtained from legal sources were found to be real. Web pharmacies not demanding prescriptions and private suppliers did however provide both oxycodone and hydrocodone that failed authentication, which may have deleterious health outcomes and suggest wider policy questions.

As Figure 6 shows, if overprescribing is reduced, in which quality is probably 100 percent, demand switches to other sources, and those other sources probably have inferior quality opioids. Larger samples and more varied sampling methods are required to confirm this result.

Figure 6. Ill-advise opioid use

⁶ In Philadelphia, 84 percent of the 1,217 fatal overdoses (in which opioids were implicated) were caused by fentanyl contamination in 2017.



Source: Author

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