

# **The Triple Wave Epidemic: Opioids, Heroin and Fentanyl: Supply Issues and Public Health Consequences**

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Chairman Smith, ranking member Bass and other distinguished members of the subcommittee on Africa, Global Health, Global Human Rights and International Organizations, thank you very much for the opportunity to testify before you today. My name is Dan Ciccarone. I am a professor of family and community medicine at the University of California, San Francisco. I have been a clinician for over 30 years and an academic researcher in the area of substance use with a focus on heroin use and the medical and public health consequences of heroin use for the past 20 years. I have been asked to speak on the public health dimensions of the fentanyl and synthetic opioid crisis in America today.

My research and that of my team is multidisciplinary and multi-level. We use the tools of epidemiology, statistics, economics, clinical and basic sciences as well as ethnography and anthropological discipline. I am appreciative of my funder, which is the National Institutes of Health, National Institute on Drug Abuse, as well as my team, which includes Dr. Jay Unick, University of Maryland, Dr. Sarah G. Mars, UCSF, Dr. Dan Rosenblum, Dalhousie University, and Dr. Georgiy Bobashev from RTI, North Carolina.

In this testimony I will discuss the rapidly-evolving intertwined epidemic of overdose due to opioid pills, heroin, and fentanyl with a focus specifically on fentanyl and other synthetic opioids. I will discuss firstly the dimension of the public health crisis. Secondly, supply-side and demand-side issues that are feeding the triple wave epidemic. I will then focus specifically on fentanyl supply and demand. Finally, I discuss possible responses.

## *A Drug Crisis of Historic Proportions*

For the first time in over two generations, the US death rate has gone up two years in a row from 2014 to 2015 and then again to 2016.<sup>1</sup> Correspondingly, life expectancy for an infant born

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<sup>1</sup> NCHS Data Brief No. 293 December 2017. U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES. Centers for Disease Control and Prevention. National Center for Health Statistics. Mortality in the United States, 2016

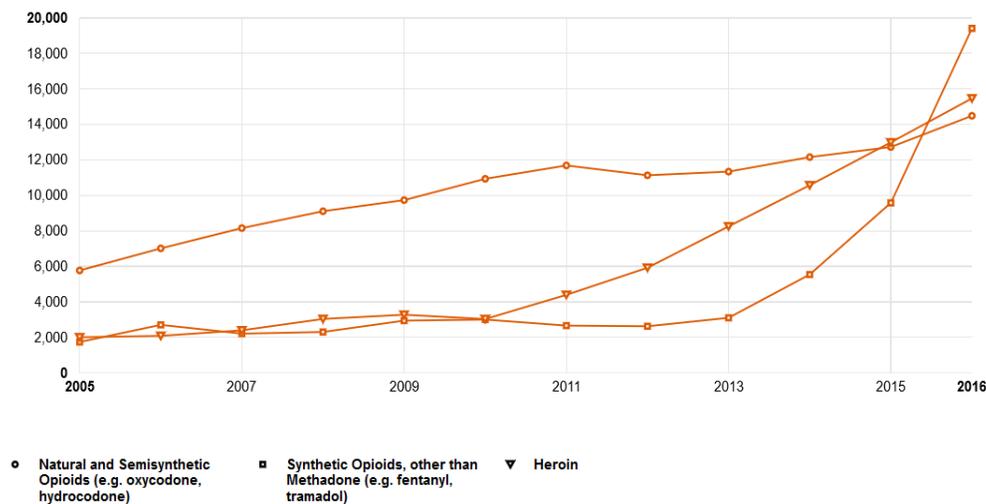
in 2015 and 2016 has also declined year over year. By examining the 10 leading causes of death, we see that heart disease and cancer, historically the top two causes of death, have maintained their positions but have gone, expectedly, down in rate. Most of the top 10 causes of death are expectedly declining year over year. However, the third leading cause of death in 2016, unintentional injuries, has been climbing the ranks following a dramatic increase in rate from 2014 to 2016.

Historically, the leading cause of unintentional injury death has been motor vehicle accidents but, as our cars have gotten safer, there's been another cause of unintentional injury that has constantly and steadily grown to surpass deaths due to motor vehicle accidents and that is deaths due to drug poisoning. Drug poisoning deaths exceeded motor vehicle deaths as of 2011 and continue to climb. According to the latest data from the US Centers for Disease Control and Prevention, deaths due to drug poisoning exceeded 72,000 in 2017.<sup>2</sup> Since the beginning of the opioid epidemic, a half a million Americans have died from drug poisoning. Annual deaths due to drug overdoses now exceed deaths due to car accidents, gun violence, and even HIV at the height of the 1990's HIV epidemic.

### *The Triple Wave Epidemic: Opioids, Heroin and Fentanyl*

The current leading cause of drug poisoning is due to the family of chemicals called opioids. We are witnessing a triple wave epidemic of overdoses from three classes of opioids: prescription pills (semi-synthetic opioids), heroin and illicitly manufactured fentanyl (synthetic opioids). Figure 1 shows three waves of opioid use and consequences, each wave cresting on top of the one before it to produce even deadlier consequences.

**Figure 1: Opioid Overdose Deaths by Type of Opioid**



Source: Kaiser Family Foundation State Health Facts / Centers for Disease Control and Prevention.<sup>3</sup>

<sup>2</sup> NCHS, National Vital Statistics System. Estimates for 2017 are based on provisional data. Estimates for 2015 and 2016 are based on final data (available from: [https://www.cdc.gov/nchs/nvss/mortality\\_public\\_use\\_data.htm](https://www.cdc.gov/nchs/nvss/mortality_public_use_data.htm)). Accessed at <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm> on September 2, 2018.

<sup>3</sup> Kaiser Family Foundation analysis of Centers for Disease Control and Prevention (CDC), National Center for Health Statistics. Multiple Cause of Death 1999-2016 on CDC WONDER Online Database, released 2017. Data are from the Multiple Cause of Death Files, 1999-2016, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed at <http://wonder.cdc.gov/mcd-icd10.html> on January 31, 2018.

The first wave, overdoses related to prescription pain medicines, started around the year 2000 and has steadily grown, according to the latest official data, through 2016. The second wave, building upon the first, are overdose deaths due to heroin, which started increasing around 2010 and continued to rise through 2016 passing the number of deaths due to opioid pills. The third wave, which is even deadlier, is that due to fentanyl, fentanyl analogues, and other synthetic opioids of illicit supply (i.e., not methadone). This wave began in 2014 and has climbed dramatically. Provisional 2017 drug overdose counts data from the National Center for Health Statistics, shows synthetic, e.g., fentanyl, opioid deaths continuing to rise, reaching a peak of almost 30,000, while semisynthetic and heroin overdose deaths level off, albeit at very high levels, approximately 15,000 per wave.<sup>4</sup>

Drug policy academics describe substance use upcycles as having two principle drivers, supply and demand; this comes out of economic theory and holds true for most consumable goods. For a drug epidemic to get to this size, it requires not just one, but both forces of supply and demand to create the enormous wave of consumption and consequences we are witnessing. First a bit of history and then I will briefly examine each of the aforementioned waves, one at a time, describing supply issues, demand issues, demographics of the population at risk, as well as some differences that exist between these three waves.

The opioid class of medications was developed to treat pain, to facilitate surgery and in general to reduce suffering at the extreme. These medications are both a miracle in their proper use, but also problematic in their misuse. Examining just this class of medications, we can consider the first epidemic of misuse and medical consequences due to morphine and heroin following their discoveries in the late 19<sup>th</sup> century.<sup>5</sup> They were novel drugs sourced through physicians and pharmacies and thus the subsequent misuse problem was iatrogenic, meaning medically caused. There was also a technological advance, the hypodermic syringe, which both advanced appropriate use, but also promoted problems related to misuse.

Heroin, diacetylmorphine, had a short life as a licit medication. We've seen a number of illicit heroin waves, beginning around the 1920's. The first of which may have been due to restriction on licit supplies driving drug use underground. We had heroin in the 1930-40's Jazz Era that had a social and cultural root to it. Moving on to the 1970's and the Vietnam Era, the heroin epidemic also had a sociocultural root to it as well as supply-driven factors including a new sources of heroin imported from Southeast and Southwest Asia. Then, in the 1990's, a new form of heroin produced by Colombian criminal trafficking organizations was brought into the United States. That new source of heroin caused a small epidemic of medical consequences.<sup>6</sup> In sum, the first century of opioids availability, including both licit, e.g. morphine and illicit e.g. heroin, opioids had a number of misuse and medical consequences waves caused by supply (iatrogenic, new illicit sources and forms) and demand forces (cultural and social, new technologies for use). Moving onto the current triple wave crisis, we see both forces at work again. Supply forces: iatrogenic source of opioid pills, a new source of technologically advanced heroin and a novel illicit opioid – fentanyl – also from a new source. Demand forces: social,

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<sup>4</sup> NCHS, National Vital Statistics System. Ibid.

<sup>5</sup> This history section is gleaned from multiple sources including: Courtwright, D.T., *Dark Paradise: A History of Opiate Addiction in America*, Cambridge: Harvard University Press, 2001. McCoy, A. W., *The Politics of Heroin*, 2<sup>nd</sup> Ed., Chicago: Lawrence Hill Books, 2003. Musto, D. F., *The American Disease: Origins of Narcotic Control*, 3<sup>rd</sup> ed., New York: Oxford University Press, 1999.

<sup>6</sup> Ciccarone D, Unick GJ, Kraus A. Impact of South American heroin on the US heroin market 1993-2004. *The International journal on drug policy*. 2009;20(5):392-401. Epub 2009/02/10. doi: 10.1016/j.drugpo.2008.12.001. PubMed PMID: 19201184; PubMed Central PMCID: PMC2719678.

cultural and economic root causes of opioid use; population dependency on opioid pills leading to spill-over effects driving heroin and subsequently, fentanyl demand.

The supply side drivers of the first wave of prescription opioid misuse and overdose have been extensively discussed in academic and policy circles. Wave one is often considered to have been driven by increased supply, i.e., a tripling of opioid prescriptions starting in the 90's and crescendoing around 2011.<sup>7</sup> This tripling of opioid prescriptions has been correlated to rising consequences, particularly overdose.<sup>8</sup> The introduction of extended release long-acting (ERLA) opioid formulations support both supply-side and demand-side pressure. ERLAs are a source of opioid in a novel form with a technological advance that allowed higher doses in a single capsule. Ease of misuse, e.g. crushing leading to insufflation (nasal 'snorting') or injection, led a wave of misuse.<sup>9</sup>

The conventional wisdom on the first wave places much the blame on the drugs involved and the sources of those drugs. A demand-side argument has been recently introduced examining the structural and social factors that might be driving the epidemic. The most compelling structural determinants include economic hardship and social and psychological malaise that may have led an at-risk population to seek opioids in the first place.<sup>10</sup>

Beginning in the late 2000's, especially by 2012, we began getting concerned about the rising number of heroin users and heroin-related overdose. Our team demonstrated a statistical relationship between the first two waves of the epidemic, opioid pills and heroin, describing them as "intertwined epidemics."<sup>11</sup> We also described how young and new heroin users at the time had transitioned to heroin from high dependency on opioid pills.<sup>12</sup> A new consciousness around the opioid pill epidemic led to a decline in physicians prescribing of opioids. Opioid pills became more difficult to get illicitly and as a consequence, a small proportion of patients found their way over to a new drug, heroin, which was more available, and at a lower price point, on the street. Thus, an unintended consequence of restrictions on opioid pill prescribing led to heroin use. There was a demand for powerful opioids that heroin fulfilled.

Data on users entering drug treatment showed that in successive cohorts from the 1960's through the 2000's, increasingly folks coming in with heroin use disorder reported starting their opioid dependency with opioid pills.<sup>13</sup> However, this has begun to change now as an increasing proportion of heroin dependent patients entering treatment report having started with heroin.<sup>14</sup> Another dramatic change occurred in late 2010, when OxyContin<sup>™</sup>, a brand name ERLA

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<sup>7</sup> Kolodny, A., Courtwright, D. T., Hwang, C. S., Kreiner, P., Eadie, J. L., Clark, T. W., & Alexander, G. C. (2015). The prescription opioid and heroin crisis: A public health approach to an epidemic of addiction. *Annual Review of Public Health*, 36, 559-574.

<sup>8</sup> CDC. Vital signs: overdoses of prescription opioid pain relievers—United States, 1999–2008. *MMWR Morb Mortal Wkly Rep* 2011;60:1487–92.

<sup>9</sup> Mars, S., Bourgois, P., Karandinos, G., Montero, F. and Ciccarone, D., Every 'Never' I Ever Said Came True: Pathways from pills to heroin injecting. *International Journal of Drug Policy*, 2014. 25(2): p. 257-266.

<sup>10</sup> Dasgupta, N., Beletsky, L., Ciccarone, D., *Am J Public Health*. 2018 Feb;108(2):182-186. doi: 10.2105/AJPH.2017.304187. Epub 2017 Dec 21. PMID:29267060

<sup>11</sup> Unick, G.J., et al., Intertwined epidemics: national demographic trends in hospitalizations for heroin- and opioid related overdoses, 1993-2009. *PLoS One*, 2013. 8(2): p. e54496.

<sup>12</sup> Mars et al. *Ibid*.

<sup>13</sup> Cicero TJ, Ellis MS. *JAMA Psychiatry*. 2015 May;72(5):424-30. doi: 10.1001/jamapsychiatry.2014.3043. PMID:25760692

<sup>14</sup> Cicero TJ, Ellis MS, Kasper ZA. *Addict Behav*. 2017 Nov;74:63-66. doi: 10.1016/j.addbeh.2017.05.030. Epub 2017 May 23. PMID:28582659

formulation of Oxycodone, was reformulated to be less abuse-able, ie less insufflatable or injectable. Because of this reformulation, that route of abuse was severely curtailed. This may be one of the triggers that increased interest in and use of illicit heroin. This reformulation of a popular drug, along with restrictions in prescribing and a new consciousness around more judicious prescribing of opioids, may in combination have had unintended consequences driving a small proportion of the at-risk population to heroin.

The first and second waves do have some contrasts in terms of demographics and regional distribution.<sup>15</sup> The age distribution of patients hospitalized for prescription opioid overdose, has its largest peaks in the 50 to 64 year old group and this has been stable for several years. In hospitalizations for heroin overdose, one sees a very different picture. The age group at highest risk are 20 to 34 year-olds with a rate of hospitalizations that is growing year by year. Another strong difference between prescription opioid overdose and heroin overdose is seen in their geographic distribution. Opioid pill overdose is relatively even across the four major US regions of the Northeast, Midwest, South and West, whereas heroin overdose is much higher, with rates of increase also higher, in the Northeast and Midwest. So, we see elements of demand-side drivers in wave two, with rising numbers of heroin users who are transitioning from prescription opioid dependency, as well as younger persons, naturally greater risk takers, initiating heroin use. In addition, there's also this notion that heroin is becoming more dangerous. Its supply is changing in quantity, source and quality and is being adulterated by synthetic opioids.

According to reports from the U.S. Drug Enforcement Administration (DEA), the U.S. heroin supply is changing dramatically, particularly during the wave two era from 2010 to 2015 in which we see an almost tripling of U.S. heroin seizures at the Southwest border.<sup>16</sup> Seizures are a proxy for supply, so as seizures go up, considering that the rate of seizure is not dramatically increasing, we assume that the supply has also expanded.

Another dramatic transformation in heroin supply, changes in sourcing, has occurred in the last 10 years. Historically imported heroin came from four source regions/countries in the world, including Southeast Asia, Southwest Asia, Mexico, and South America. In the 2000's we began an era in which most of our heroin came solely from two sources: Colombian and Mexican criminal trafficking organizations (CTOs).<sup>17</sup> Accelerating this trend towards fewer sources, since the mid 2000's to present, Mexican CTO's have increasingly dominated the U.S. heroin market; with 50% market share in 2005 and growing to 90% with the latest data.<sup>18</sup>

Mexican-sourced heroin is also becoming more refined. DEA documents reveal, that for a period of time in the late 2000's and early 2010's, that a substantial proportion of heroin samples were from an unknown source and of unknown quality.<sup>19</sup> This is now better understood as heroin sourced from Mexican CTOs, but is of a different, more refined, chemical composition than previous Mexican-sourced heroin. DEA reports highlight the evidence that the Mexico-based

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<sup>15</sup> Unick GJ, Ciccarone D. US regional and demographic differences in prescription opioid and heroin-related overdose hospitalizations. *Int J Drug Policy*. 2017 Aug;46:112-119. doi: 10.1016/j.drugpo.2017.06.003. Epub 2017 Jul 5. PMID:28688539

<sup>16</sup> National Seizure System. Reported in the *2016 National Heroin Threat Assessment Summary*; DOJ, DEA, 2016

<sup>17</sup> Update: Heroin Signature Program. Reported in the *2015 National Drug Threat Assessment Summary*; DOJ, DEA, 2015

<sup>18</sup> Drug Enforcement Administration, *2017 National Drug Threat Assessment*, DEA-DCTDIR-040-17, October 2017.

<sup>19</sup> Source: Domestic Monitoring Program. Reported in the *2015 National Drug Threat Assessment Summary*; DOJ, DEA, 2015

Sinaloa Cartel in particular has control of the U.S. heroin retail market, with particular domination in the Midwest, Mid-Atlantic and New England regions.<sup>20</sup>

In summary, there are significant supply-side forces behind rising heroin overdose – wave two – that we see in the Midwest, Mid-Atlantic, and New England areas. Mexican-sourced opium and heroin production has grown dramatically trading off with Colombian production. A more refined product coming from Mexico, so-called “Mexican White” heroin, which is a Colombian mimic, is going to areas where, traditionally, Colombia-sourced heroin has gone; this perhaps under the control of the Sinaloa CTO.

That brings us to the third wave, fentanyl and synthetic opioids in the heroin market.<sup>21</sup> Fentanyl is a synthetic opioid, i.e. a chemical manufactured in a pharmaceutical facility. This is different than, for example, morphine, which is a natural product derived from the opium poppy plant. It also distinguishes it from several other highly used pain medications like oxycodone and hydrocodone, which are semi-synthetic opioids derived from chemical constituents of the poppy plant, but then altered to make them more useful as pharmaceuticals. Heroin, which is diacetylmorphine, is also a semi-synthetic.

Fentanyl is a well-regarded pharmaceutical, used in surgery and to control severe pain. It's short-acting, so physicians and surgeons can dose it with a lot of control. On the other end of the spectrum, it can be used as a long-acting patch, in which the embedded fentanyl slowly enters the body; this is considered a boon to both chronic pain and hospice patients.

The fentanyl we are discussing today is not a diverged pharmaceutical product, it is an illicitly manufactured, clandestinely distributed fentanyl.<sup>22</sup> This fentanyl is integrated into the illicit drug supply and sold as “heroin” in powder form, or as counterfeit opioid or benzodiazepine pills. It is rarer, particularly on the street, that it is being sold as-is. Its intentional use is far outweighed by non-intentional use, that is, street users of illicit opioids are looking for heroin, or opioid pills, and the fentanyl comes along as an unexpected contaminant. Fentanyl is a highly potent drug, about 80-100 times as strong as morphine by weight, which makes it 30-40 times stronger than heroin by weight.

Heroin, particularly in the region with the greatest increases in wave two overdose, i.e. the Midwest, Mid-Atlantic and New England regions, exists as a *fentanyl-substituted and/or fentanyl-adulterated heroin*.<sup>23</sup> There is also increasing concerns of fentanyl contamination of the street market in methamphetamine and cocaine.

Fentanyl is the main chemical in a growing family of chemicals.<sup>24</sup> The central chemical – fentanyl – is also the main one of concern. However, there is also a growing family of analogues, which are like chemical cousins, to the fentanyl molecule. They would include such things as

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<sup>20</sup> Domestic Monitoring Program. Reported in the 2015 National Drug Threat Assessment Summary; DOJ, DEA, 2015

<sup>21</sup> Ciccarone D. Fentanyl in the US heroin supply: A rapidly changing risk environment. *Int J Drug Policy*. 2017 Aug;46:107-111. doi: 10.1016/j.drugpo.2017.06.010. Epub 2017 Jul 20. PMID:28735776

<sup>22</sup> Gladden RM, Martinez P, Seth P. Fentanyl Law Enforcement Submissions and Increases in Synthetic Opioid-Involved Overdose Deaths - 27 States, 2013-2014. *MMWR Morb Mortal Wkly Rep*. 2016 Aug 26;65(33):837-43. doi: 10.15585/mmwr.mm6533a2.

<sup>23</sup> Ciccarone D, Ondocsin J, Mars SG. Heroin uncertainties: Exploring users' perceptions of fentanyl-adulterated and -substituted 'heroin'. *Int J Drug Policy*. 2017 Aug;46:146-155. doi: 10.1016/j.drugpo.2017.06.004. Epub 2017 Jul 18. PMID:28735775

<sup>24</sup> Suzuki J, El-Haddad S. A review: Fentanyl and non-pharmaceutical fentanyls. *Drug Alcohol Depend*. 2017 Feb 1;171:107-116. doi: 10.1016/j.drugalcdep.2016.11.033. Epub 2016 Dec 16. Review. PMID:28068563

acetyl fentanyl and furanyl fentanyl, etc. The fentanyl analogues come in a range of morphine-equivalent potencies with some, e.g., acetyl-fentanyl being less potent than fentanyl by weight, while others have greater potency.

In addition to fentanyl and its analogues there are additional novel synthetic opioids that we are concerned about including U47700 and U48800, as well as others. The biggest concern is around a branch of the fentanyl family that includes some incredibly powerful medications including carfentanil, alfentanil, and sufentanil, which are exceedingly potent. It is unclear whether these super-high potency fentanyls will take off in the marketplace, or if they are just ‘accidents’ in the rapidly evolving illicit opioid supply.

According to the DEA, the main source of illicitly manufactured fentanyl is China.<sup>25</sup> Fentanyl sourced from China takes a number of routes on its way into the U.S. It is shipped directly into the United States in powdered form and sold as heroin, or pressed into counterfeit opioid pills and sold. It is also shipped into Canada, where it is sold domestically as heroin or pressed into pills and exported to the U.S. However, perhaps the largest part segment of this illicit market, is fentanyl that is shipped to Mexico, where it is then processed by the Mexican CTOs and either cut into heroin or transshipped with heroin for mixing in the regional markets of the U.S.

According to testimony given by Richard Baum, former Acting Director Office of National Drug Control to the Congressional Committee on Energy and Commerce, March 29, 2017, an estimated 668 kilograms of illicitly manufactured fentanyl, bound for the U.S. market was seized in 2016.<sup>26</sup> There is both CTO distribution of fentanyl in the United States, as well as individual and entrepreneurial distribution. The former is typically large scale with low purity product; the latter is small scale, often shipped through the postal system, albeit with high purity product. Fentanyl seizures stemming from screening of inbound international mail by Customs and Border Protection included 15 kilograms of inbound international mail and 21 kilograms from express mail carriers. In addition, Department of Homeland Security reported seizing 58 illicit pill pressing machines in 2016.

What is most telling, in terms of supply, about the third wave fentanyl epidemic is how regionally discrete it is in the United States. Comparing drug seizure data, from the DEA, with overdose death data, from the CDC, one finds remarkable geographical correlation between fentanyl seizures and fentanyl-related overdoses.<sup>27</sup> We see this overlap in the Midwest, e.g., Ohio, Pennsylvania, and down into Appalachia, e.g., Kentucky and West Virginia. We see it in the Mid-Atlantic region, e.g., New Jersey, and then up into England, e.g., New Hampshire and Massachusetts. Where the fentanyl is distributed is where the fentanyl-related deaths are. This strong regional distribution suggests, with support from DEA reports, that a large supply player or players are involved. If the epidemic of fentanyl overdose was more evenly spread around the country it would support the notion that the supply was entrepreneurially driven, e.g., people interested in fentanyl were finding it on the dark web and shipping it to their individual locations; that perhaps it is a culturally driven, or demand-driven event. The fact that it is so regional is evidence that illicitly manufactured fentanyl is predominately cartel CTO-driven; that this is a supply-side event. The DEA has in some of their documents agreed that the Sinaloa Cartel

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<sup>25</sup> Drug Enforcement Administration, *2016 National Drug Threat Assessment*, DEA-DCTDIR-001-17, November 2016.

<sup>26</sup> Baum, R J. 2017. Letter to Congress: Response to questions concerning fentanyl. Washington DC: Office of National Drug Control Policy.

<sup>27</sup> Gladden RM, et al. *Ibid*

seems to be heavily implicated.<sup>28</sup> We need to keep in mind that there are fentanyl and other synthetic opioid deaths elsewhere in the country, e.g., rising fentanyl-related overdose deaths in California are a growing concern, albeit of lower magnitude than in the most impacted regions.

I mentioned in the earliest part of my testimony that my team and I use ethnographic techniques in our research, which means we have the privilege of talking to people who are most impacted by this epidemic. We document their stories of how they are coping with changes in the drug supply, the decisions they are making, what they like and what they don't like about the drugs, and what kind of help they most want. They confirm that the changes in heroin due to its substitution by, or adulteration with fentanyl have been disturbing to them. That fentanyl was not a demand-driven phenomenon. There is currently a range of desirability for fentanyl, but this is only after several years of its constant presence in the heroin supply.<sup>29</sup>

One piece of evidence supporting the lack of demand for fentanyl is the lack of cultural idioms for fentanyl. Most desired illicit drugs have a slang for them. There is no slang developed yet for fentanyl despite four years of steady supply.

In addition to the dangerous potency of fentanyl, our ethnographic observations support the notion of a possibly greater danger: rapid changes in purity, as well as different mixtures of heroin and fentanyl and its analogues.<sup>30</sup> These vicissitudes, we may discover, may have profound effects on the overdose rate in a given location.

In summary of this description of the supply-side and demand-side drivers of the triple-wave epidemic, we have to consider whether this is one intertwined epidemic, or three separately evolving epidemics. The geographic, demographic, and supply disparities seen in the data confound any simple story. All three waves have impressive supply-side drivers including excessive medication prescribing, new forms of Mexican-sourced heroin and a new illicit source of opioid, Chinese-sourced synthetics adulterating heroin and counterfeit pills. Demand for opioid pills drove demand, both directly and indirectly, for heroin; demand for heroin indirectly feeds demand for synthetics-as-substitute. What is driving increases in opioid mortality now are deaths due to heroin and heroin adulterated by fentanyl. The second and third waves are regional, with the Midwest, Northeast, Mid-Atlantic and Appalachia regions affected the most.

There are other medical consequences, in addition to overdose, that are growing in concern. The change from pill misuse to heroin involved, for many, a change in route of administration. Pills tend to be swallowed although, as mentioned above, with ERLA oxycodone misuse some people were crushing them and insufflating or injecting the powder. Heroin, while it can be smoked or insufflated tends, in the U.S., to be injected. As the at-risk population shifts from oral misuse to injection we have to be cognizant of the infectious disease risk, including that due to blood-borne viruses such as hepatitis C and HIV. The U.S. has now had two documented injection-drug-related HIV epidemics, Scott County, Indiana,<sup>31</sup> and more recently in Massachusetts.<sup>32</sup> In addition to blood-borne viruses, we have to be concerned about injection-related bacterial infections such as endocarditis and skin and soft tissue infections.

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<sup>28</sup> DEA, 2017. Ibid.

<sup>29</sup> Ciccarone D., et al., 2017. Ibid

<sup>30</sup> Ciccarone D., 2017. Ibid

<sup>31</sup> P.J. Peters, P. Pontones, K.W. Hoover, M.R. Patel, R.R. Galang, J. Shields, et al. for the Indiana HIV Outbreak Investigation Team (2016). HIV infection linked to injection use of oxycodone in Indiana, 2014–2015. *The New England Journal of Medicine*, 375 (2016), pp. 229-239

<sup>32</sup> CDC, Epi-Aid Number: 2018-027. *Undetermined Risk Factors and Mode of Transmission for HIV Infection Among Persons Who Inject Drugs — Massachusetts, 2018*. July 17, 2018

## *Addressing the Fentanyl Crisis*

We can see this triple-wave epidemic as an intertwined, three drug epidemic, but to comprehend it fully we need to appreciate the drivers of each wave. We have noted how supply shocks can lead to drug epidemics both historically and in the current opioid crisis. Fentanyl in particular comes as a strong supply shock leading to disastrous consequences. Thus it is tempting to focus our efforts on controlling supply. We can examine supply control as one answer, but it must be one part of a more complex answer. The evidence shows that supply-side interventions can work if part of a comprehensive program that also includes demand reduction.<sup>33</sup> Unipolar supply-side interventions may actually cause paradoxical, unwanted results.<sup>34</sup> We may have already seen these phenomena within the current crisis. Downward pressure on opioid prescribing may be driving a portion of the at-risk population from opioid pill misuse to heroin, thus exposing them to the even more dangerous chemical family of fentanyls. Another driver of unintended consequences may have been the reformulation of ERLA opioids to abuse-deterrent formulations, examples of which include OxyContin™ and Opana™, another ERLA, misuse of which has been implicated in the Scott County Indiana HIV outbreak.<sup>35</sup> This is not to say that we should not pursue these goals of creating abuse-deterrent formulations or curtailing excessive prescribing practices. As we do these things we must also consider the consequences of our actions and respond accordingly.

## *Supply-Side Interventions*

Considering the inadequate and paradoxical effects of current opioid supply interventions, we must broaden our supply-side policies to cover the range of illicit opioid flows and – *crucially* – combine these efforts with expansion of effective drug treatment and harm reduction.<sup>36</sup> Regarding fentanyl, supply-side interventions includes source control and interdiction in the drug supply chain. Considering source control, we need to work diplomatically and politically with representatives from the Chinese government and find incentives to have them curtail the production and export of fentanyl and other synthetic opioids. Interdiction will be challenging given the size of the fentanyl flows. In 2016 an estimated 668 kilograms of fentanyl was seized in the US.<sup>37</sup> This is but a fraction of the estimated 11 metric tons of cocaine seized, just at the U.S. Southwest Border, in 2016.<sup>38</sup> Fentanyl is a drug which has high potency in small volumes. Considering a seizure to importation ratio of 1:4, a total of 2.6 metric tons of fentanyl are distributed – per year – for the whole U.S. This would fit into approximately 10 industrial drum barrels. And that’s a small volume that if divided up over the

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<sup>33</sup> Caulkins, J.P., Reuter, P., Iguchi, Y.P., Chiesa, J. *How Goes the “War on Drugs”? An Assessment of U.S. Drug Problems and Policy*. RAND Drug Policy Research Center, 2005.

<sup>34</sup> Ciccarone, et al, 2009. Ibid.

<sup>35</sup> Broz D, Zibbell J, Foote C, Roseberry JC, Patel MR, Conrad C, Chapman E, Peters PJ, Needle R, McAlister C, Duwve JM. Multiple injections per injection episode: High-risk injection practice among people who injected pills during the 2015 HIV outbreak in Indiana. *Int J Drug Policy*. 2018 Feb;52:97-101. doi:10.1016/j.drugpo.2017.12.003.

<sup>36</sup> Pacula RL and Powell D. A supply-side perspective on the opioid crisis. *Journal of Policy Analysis and Management*. 2018 DOI: 10.1002/pam

<sup>37</sup> Baum, 2017. Ibid.

<sup>38</sup> Drug Enforcement Administration, *Colombian Cocaine Production Expansion Contributes to Rise in Supply in the United States*, DEA Intelligence Brief, DEA-DCI-DIB-014-17, August 2017.

huge trade that occurs across the Pacific Rim constitutes a proverbial needle in a haystack of detection.

In drug policy theory there a famous notion of the balloon hypothesis, i.e., by squeezing drug supply too harshly in one direction it simply balloons out with a different source, or a different drug, routed to a different area. The concern is if we constrain fentanyl, i.e., the mother chemical, too robustly and too rapidly, it will foster the supply in fentanyl analogues. The number of known fentanyl analogues exceeds 60; the number of potential fentanyl analogues could exceed 600. We need to be careful not to foster the ingenuity and creativity of the illicit drug manufacturers to push in even more dangerous directions.

### *Surveillance of the Drug Supply*

One supply-side intervention with potential wide impact is drug surveillance. Investments in drug monitoring, identification and data collection could assist in interdicting supply.<sup>39</sup> There is an opportunity here, with the rapidly evolving synthetic opioids, to improve our surveillance techniques so that we can better detect the chemicals, their flows and their mixtures. Of crucial import: how rapidly are those substances, flows, and mixtures changing? Surveillance is a crucial and underplayed card in our hand of options in addressing this crisis. Government officials have called for greater public safety and public health collaboration to address this crisis. One way for these two domains to work together is by increasing drug surveillance – *and sharing of the data*. Improved surveillance would benefit not just folks on the interdiction and public safety side, but also the public health side including first responders, emergency and hospital clinicians as well as those who work in community based programs serving the affected population.<sup>40</sup>

### *Demand Reduction*

In summary, complex problems require complex solutions. We need combined approaches to reduce the unintended consequences of unipolar actions. In addition to putting our creativity and ingenuity into supply side detection, surveillance, interdiction and diplomatic supply control strategies, we also need to heavily invest in demand reduction, which would include prevention, medical substance use treatment and harm reduction. Opioid use disorder has a number of medical treatment options that have been shown to be effective as well as cost-effective.<sup>41</sup> Opiate agonist therapy with methadone and buprenorphine has been shown to be efficacious when coupled with high quality and low barrier treatment programs. We also must also consider the benefits of harm reduction programs. The Surgeon General has called for greater distribution of naloxone, the opioid antagonist used to treat an opioid, heroin or fentanyl overdose.<sup>42</sup> Getting wider distribution of naloxone into the community is an essential strategy in the current epidemic. Other harm reduction strategies include sterile syringe provision and supervised consumption spaces to aid in prevention of overdose and HIV and HCV transmission. These

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<sup>39</sup> Pacula and Powell, 2018. Ibid

<sup>40</sup> Ciccarone, IJDP, 2017. Ibid

<sup>41</sup> N.D. Volkow, T.R. Frieden, P.S. Hyde, and S.S. Cha, "Medication-Assisted Therapies—Tackling the Opioid-Overdose Epidemic," *New England Journal of Medicine*, Vol. 370, No. 22, 2014.

<sup>42</sup> Surgeon General's Advisory on Naloxone and Opioid Overdose. U.S. Department of Health and Human Services. 2018. Accessed: <https://www.surgeongeneral.gov/priorities/opioid-overdose-prevention/naloxone-advisory.html>

services can provide a hub or magnet for persons at risk and provide them with the resources and referrals to services.

This is a crisis that requires crisis level response. We know that government intervention and funding can help. The HIV crisis of the 1990's provides a shining example of government intervention assisting to curtail a crisis. The Ryan White Care Act led to a dramatic increase in funding for HIV prevention and treatment. That coupled with scientific and medical progress on treatment and prevention led to a dramatic decrease in HIV incidence, prevalence, morbidity, and mortality. The costs of the current triple opioid crisis are enormous, some estimates approach 80 billion per year, and the costs to address it are ultimately likely to be very high. Estimates range from \$60 billion for treatment over the next 5 years<sup>43</sup> to \$100 billion for a multi-pronged approach to prevention, treatment and community resilience efforts.<sup>44</sup>

Thank you for inviting me and listening to my testimony. I welcome the opportunity to answer your questions.

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<sup>43</sup> Simmons A. M. White House commission recommends president declare a national emergency over the deadly opioid epidemic. Los Angeles Times, Jul 31, 2017. <http://www.latimes.com/nation/la-na-opioids-commission-report-20170731-story.html>

<sup>44</sup> Katz, K. How a police chief, a governor and a sociologist would spend \$100 billion to solve the opioid crisis. The Upshot, New York Times, Feb 14, 2018. <https://www.nytimes.com/interactive/2018/02/14/upshot/opioid-crisis-solutions.html>