

Heroin & Other Illicit Drugs Track

America's Hidden Drug Epidemic: It's More than Opioids

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Disclosures

- Thom Browne, Jr., MA; David Martin, PhD; and Mark D. Birdwhistell, MPA, have disclosed no relevant, real, or apparent personal or professional financial relationships with proprietary entities that produce healthcare goods and services.
- Mark S. Gold, MD – Consulting fee: RiverMend Health

Disclosures

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 - Kelly J. Clark, MD, MBA, FASAM, DFAPA – Consulting fees: Braeburn, Indivior

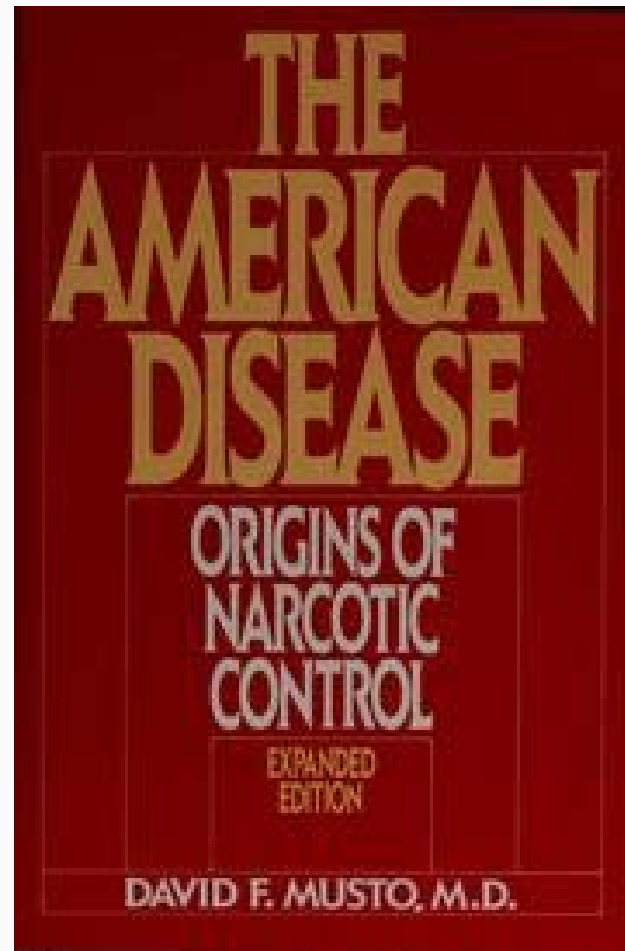
Learning Objectives

- Identify the major toxic adulterants appearing in heroin.
- Explain the health-related effects of individual toxic adulterants.
- Recognize the importance of evaluating overdose victims for exposure to adulterants.

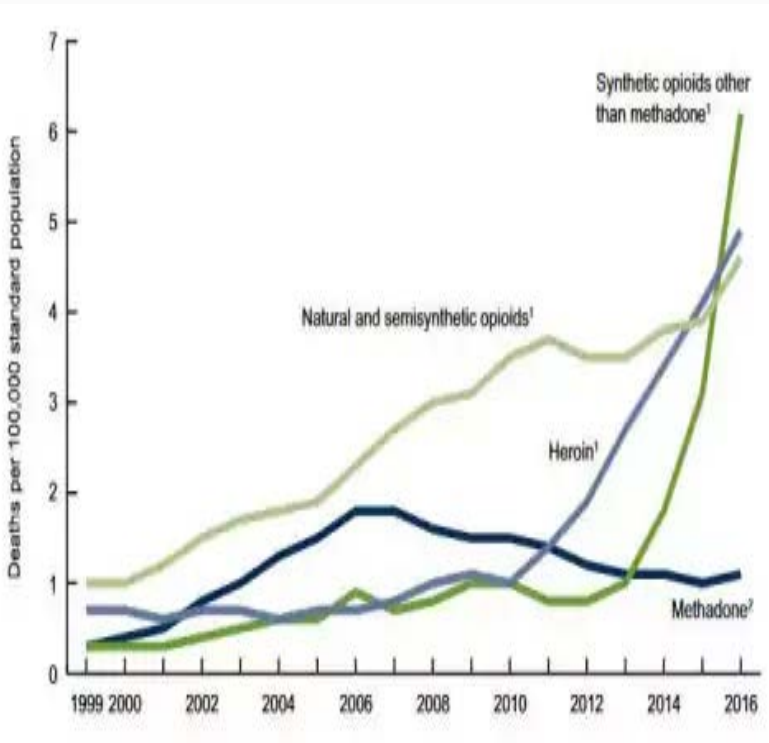
Yale Doctor Discovers New Heroin Treatment



Dr. Mark S. Gold, chief resident of the research unit in the Department of Psychiatry at the Yale Medical School, examines a color slide in preparation for a presentation he is giving today before the National Academy of Sciences' special section on drug abuse meeting in Baltimore.



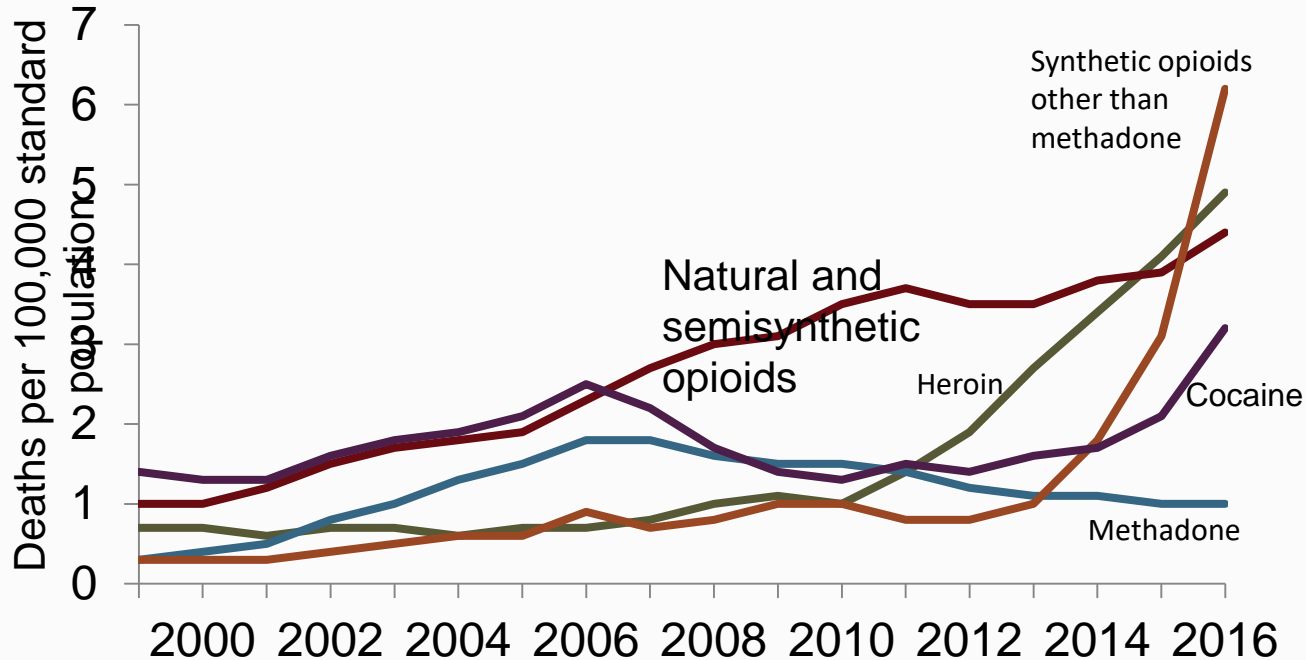
Life Expectancy Drops Again As Opioid Deaths Surge In U.S.



- Some researchers studying mortality trends say the opioid epidemic is just part of a larger problem.
- "It's also a crisis in which people are killing themselves in much larger numbers — whites especially," says Anne Case, an economist at Princeton University who has been studying what she and her husband and fellow Princeton economist Angus Deaton call "Deaths of Despair."
- "Deaths from alcohol have been rising as well. So we think of it all being signs that something is really wrong and whatever it is that's really wrong is happening nationwide," Case says.
- The decline of well-paying jobs with significant yearly salary increases, job security and good benefits may be fueling a sense of frustration and hopelessness, Case says. That may be one reason fewer people are getting married and more people are having children outside of marriages, Case says.
- "They don't have a good job. They don't have a marriage that supports them. They may have children that they do or don't see," Case says. "They have a much more fragile existence than they would have had a generation ago."
- As a result, "it may be the deaths from drugs, from suicide, from alcohol are related to the fact that people don't have the stability and a hope for the future that they might have had in the past," Case says.

Age-adjusted drug overdose death rates, for selected drugs,

United States, 1999-2016

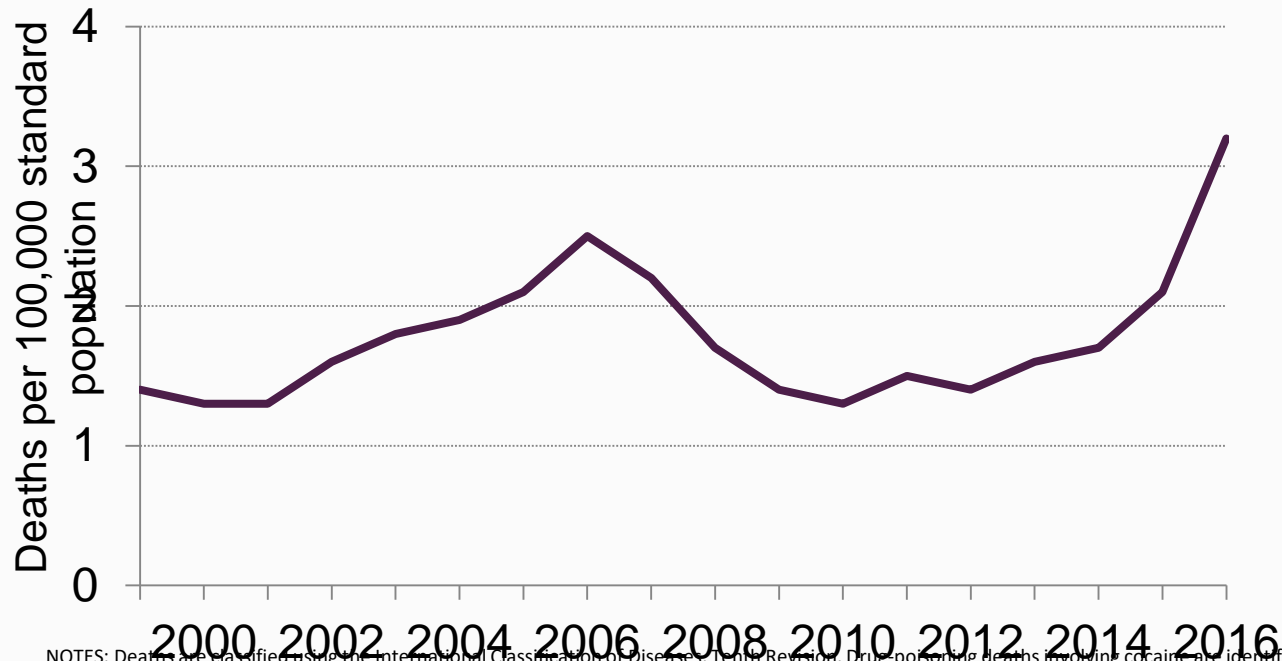


NOTES: Deaths are classified using the International Classification of Diseases, Tenth Revision. Drug-poisoning deaths are identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Drug overdose deaths involving selected drug categories are identified by specific multiple-cause-of-death codes: heroin, T40.1; natural and semisynthetic opioids, T40.2; methadone, T40.3; synthetic opioids other than methadone, T40.4; cocaine, T40.5. Deaths involving more than one drug (e.g., a death involving both heroine and cocaine) are counted in both categories. The percentage of drug overdose deaths that identified the specific drugs involved varied by year ranging from 75-79% from 1999 through 2013 and from 81-85% from 2014 through 2016.

SOURCE: NCHS, National Vital Statistics System Mortality File.

Age-adjusted rates for drug overdose deaths involving cocaine

United States, 1999-2016

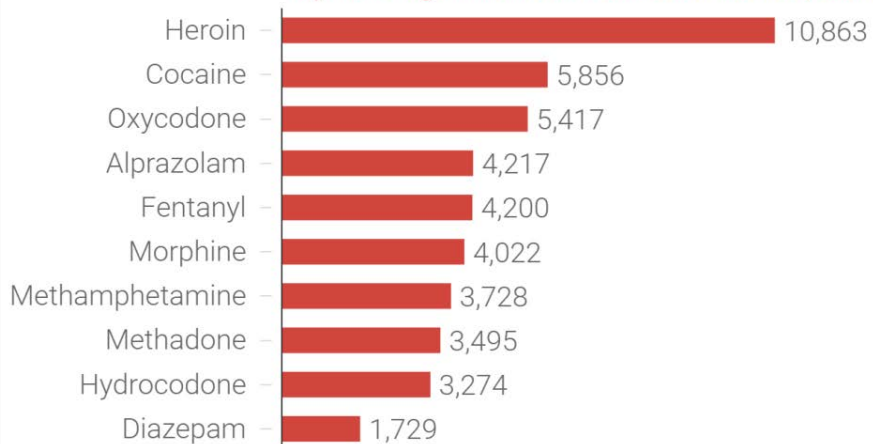


NOTES: Deaths are classified using the International Classification of Diseases, Tenth Revision. Drug-poisoning deaths involving cocaine are identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14 and multiple-cause-of-death code T40.5. The percentage of drug overdose deaths that identified the specific drugs involved varied by year ranging from 75-79% from 1999 through 2013 and from 81-85% from 2014 through 2016.

SOURCE: NCHS, National Vital Statistics System Mortality File.

Drug Deaths in the USA---Cocaine is #2

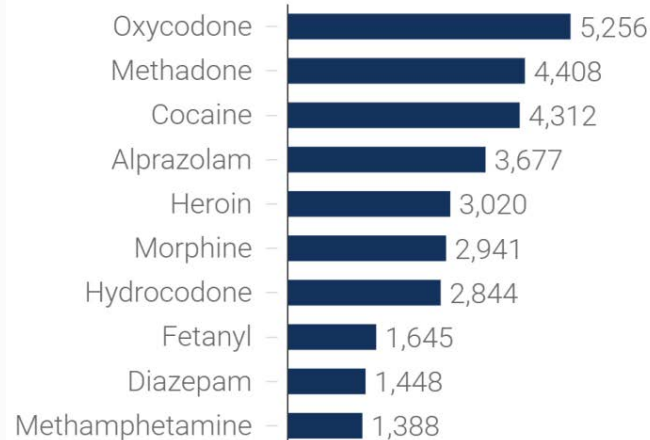
Top 10 Drugs Involved in Overdose Deaths, 2014



Made with Chartbuilder

Data: CDC; By Kimberly Leonard for USN&WR

Top 10 Drugs Involved in Overdose Deaths, 2010



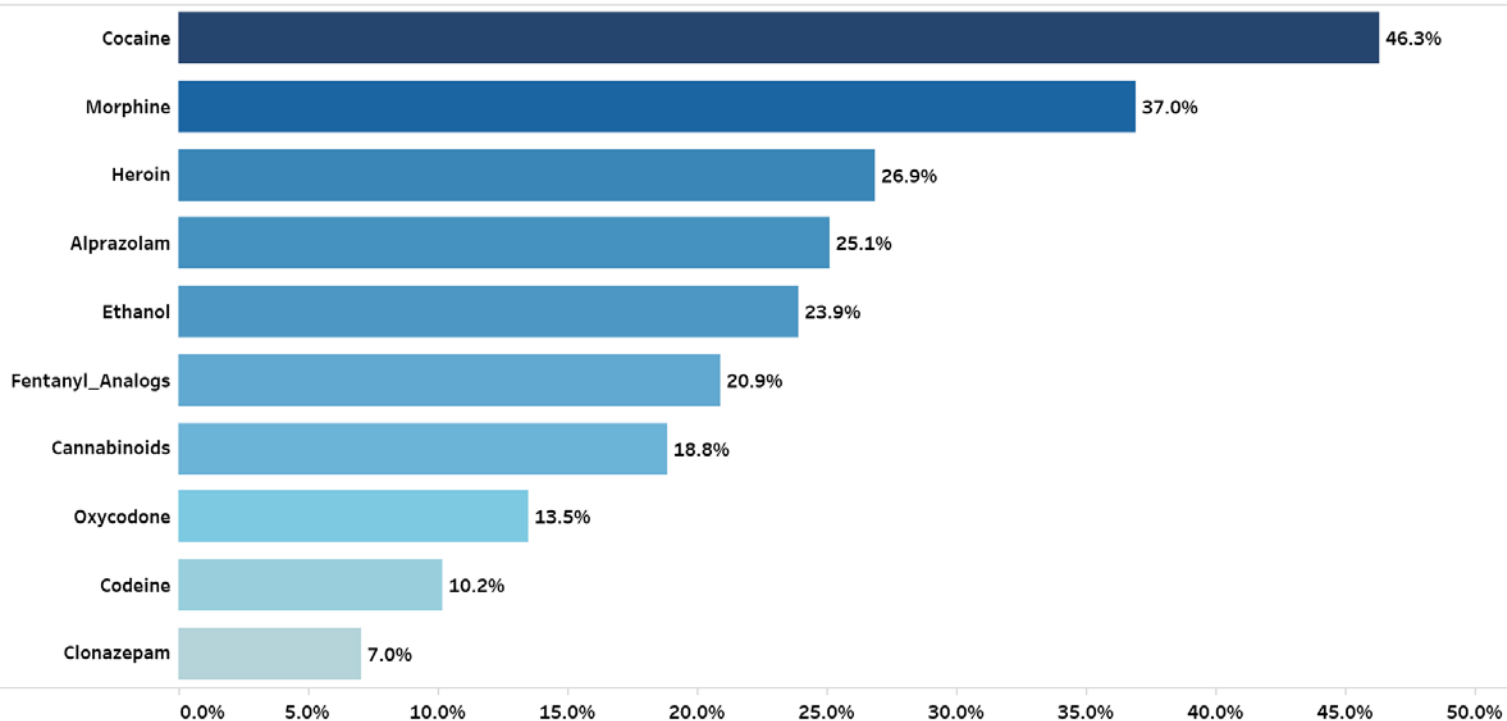
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Data: CDC; By Kimberly Leonard for USN&WR

State of Florida Fentanyl-Related Deaths (N=1391)

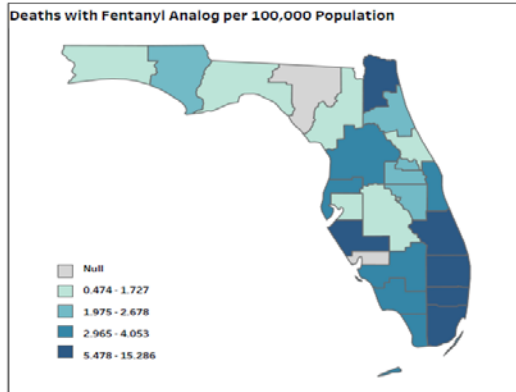
Bruce Goldberger, Ph.D.

Top 10 Co-occurring Substances among Fentanyl-Caused Deaths in 2016



Florida drug-Related Outcomes Surveillance and Tracking (FROST) University of Florida

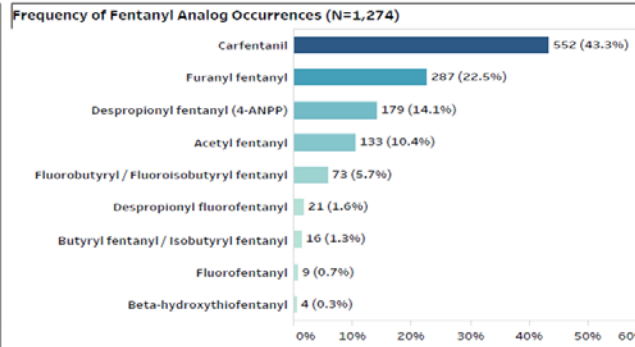
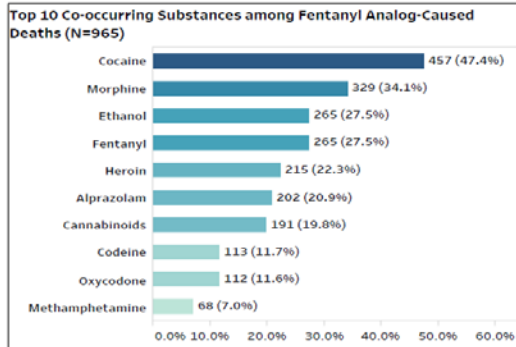
Deaths with Fentanyl Analog in 2016



Deaths with Fentanyl Analog	Cause	Present	Grand Total
In Combination with Other Drugs	871	60	931
Only	94	1	95
Grand Total	965	61	1,026

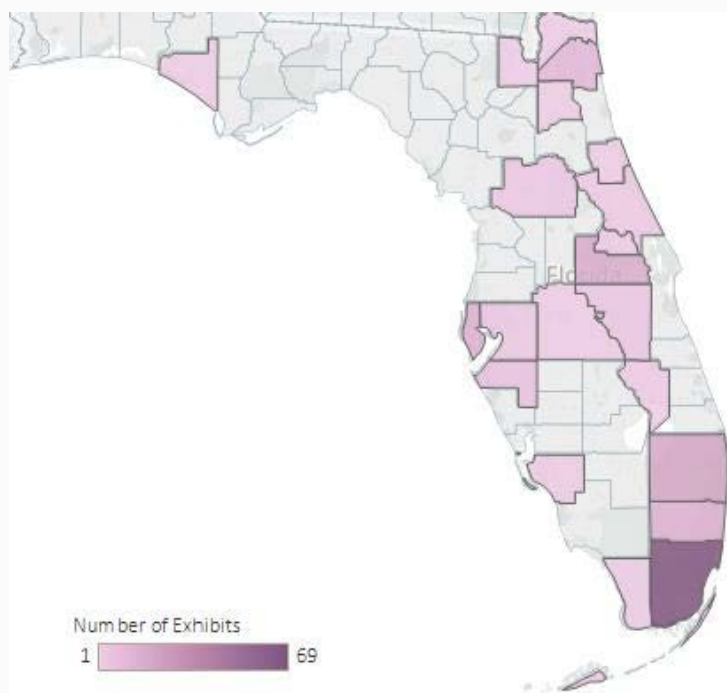
	Cause or Present?				
	All				
	Age Group				
	<18	18-25	26-34	35-50	>50
Deaths	1	129	353	369	174
% of Total	0.10%	12.57%	34.41%	35.96%	16.96%

	Manner of Death				
	Accidental	Suicide	Homicide	Natural	Undetermined
Deaths	1,014	7	3	1	1
% of Total	98.83%	0.68%	0.29%	0.10%	0.10%



Funding provided by BJA, DOJ

Seized Cocaine Containing Fentanyl, Carfentanil



- The widespread seizures of contaminated cocaine indicate that drug dealers are commonly mixing fentanyl and fentanyl-related substances into the drug.
- In some cases, this is done purposefully to increase the drug's potency or profitability. In other cases, fentanyl is inadvertently mixed into cocaine by drug dealers using the same blending equipment to cut various types of drugs, such as heroin.
- Regardless, the adulteration often occurs without the users' awareness, which leads to overdose incidents. Individuals who use cocaine occasionally are at an extremely high risk of overdose.

Recent Increases in Cocaine-Related Overdose Deaths and the Role of Opioids

- **Objectives.** To assess trends in cocaine overdose deaths and examine the role opioids play in these deaths.
- **Methods.** We used data on drug overdose deaths in the United States from 2000 to 2015 collected in the National Vital Statistics System to calculate annual rates and numbers of cocaine-related overdose deaths overall and deaths both involving and not involving opioids. We assessed statistically significant changes in trends with joinpoint regression.
- **Results.** Rates of cocaine-related overdose deaths increased significantly from 1.26 to 2.50 per 100 000 population from 2000 to 2006, declined to 1.35 in 2010, and increased to 2.13 in 2015. Cocaine-related overdose deaths involving opioids increased from 0.37 to 0.91 from 2000 to 2006, declined to 0.57 in 2010, and then increased to 1.36 in 2015. Cocaine-related overdose deaths not involving opioids increased from 0.89 to 1.59 from 2000 to 2006 and then declined to 0.78 in 2015. **Conclusions.** Opioids, primarily heroin and synthetic opioids, have been driving the recent increase in cocaine-related overdose deaths. This corresponds to the growing supply and use of heroin and illicitly manufactured fentanyl in the United States.
- Cocaine-related overdose deaths increased significantly between 2000 and 2006. Between 2006 and 2010, consistent with a reduction in supply and an increase in street prices. The public health and public safety response to increasing cocaine-related overdose deaths should be comprehensive and informed by the role opioids play. This is particularly important given the rapid increase in cocaine-related deaths involving synthetic opioids such as fentanyl and its highly potent analogs.
- . (Am J Public Health. 2017;107:430–432. doi:10.2105/AJPH.2016.303627)

Adulterants--- Poisonings

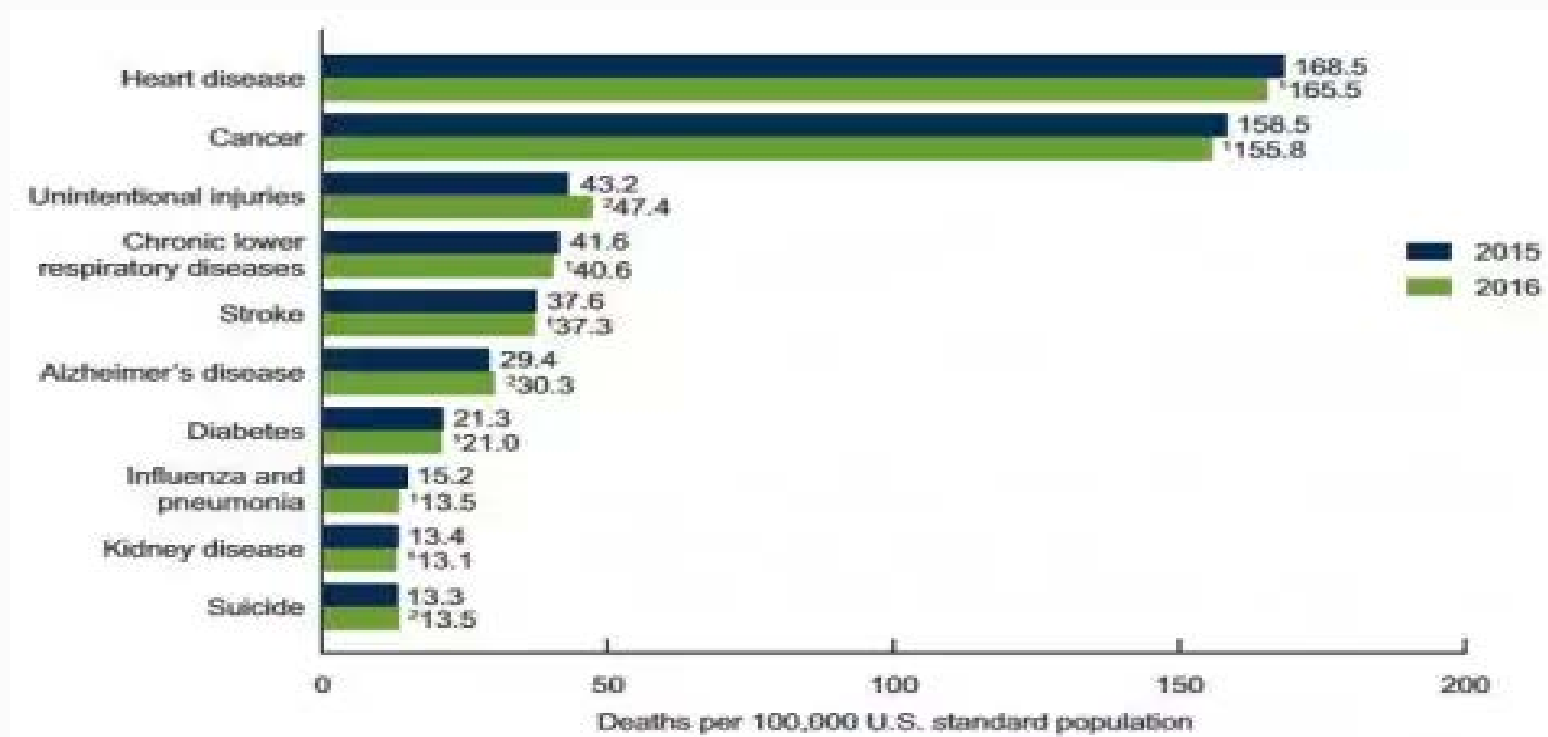
- "The large majority (87%) of cocaine bricks contained levamisole and/or levamisole mixtures with dexamisole, while only one percent of bricks contained various other cutting agents“



- page 84 DEA 2017 National Drug Threat Assessment
- https://www.dea.gov/docs/DIR-040-17_2017-NDTA.pdf

10 leading causes of death, significant increases last year came in unintentional injuries (which include drug overdoses), Alzheimer's disease and suicides

(2017- CDC National Center for Health Statistics)



“Missed Opportunities: Opioid Overdoses and Suicide”

A. Benjamin Srivastava MD and Mark S. Gold, MD

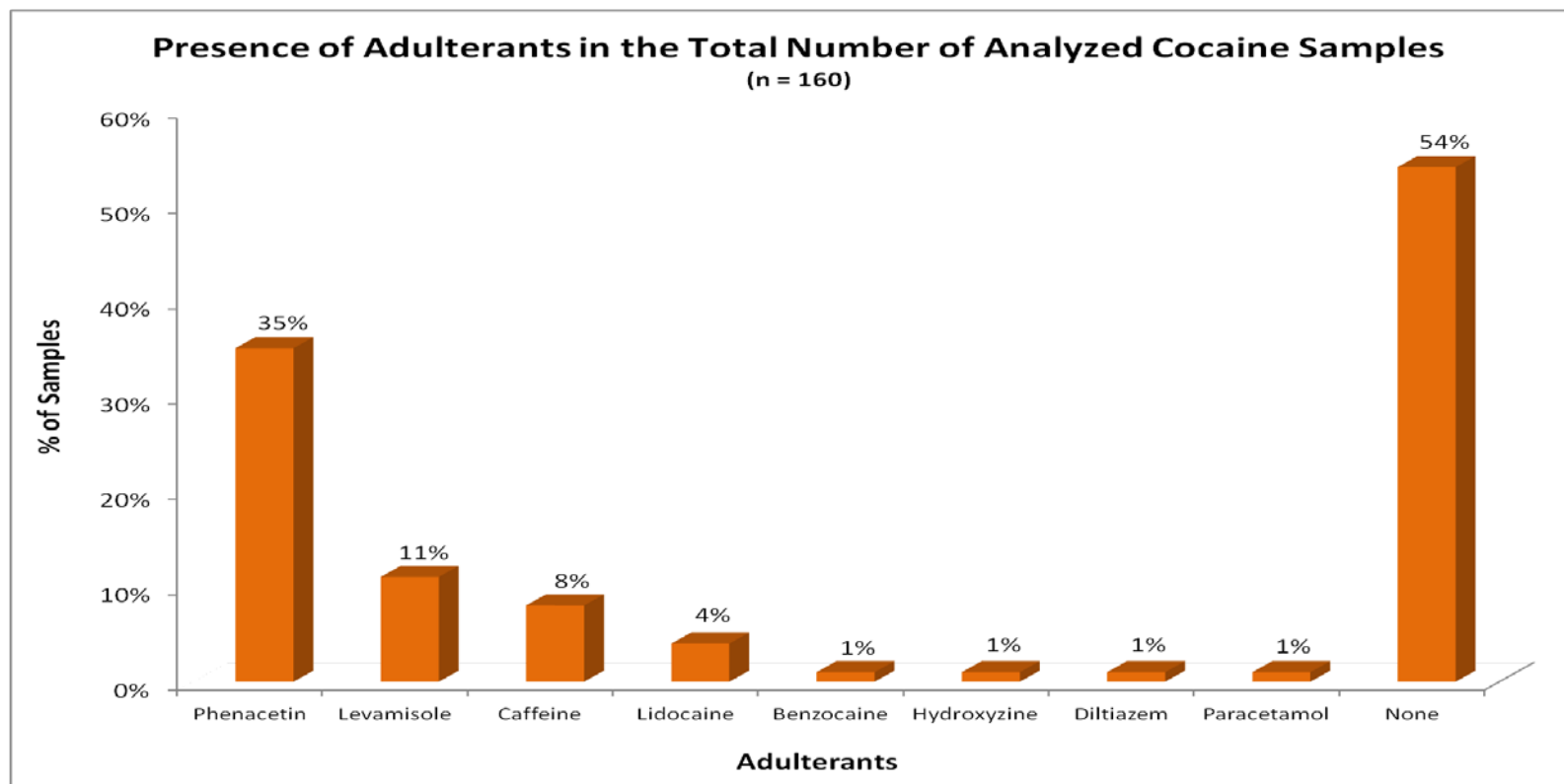
- ..more than 50% of patients with opioid use disorder have histories of major depressive disorder, which, when untreated, may further drive suicidal thoughts and behavior.^{10,11} Maria A. Oquendo, MD, PHD, immediate past president of the American Psychiatric Association, wrote in a guest post on the blog of Nora D. Volkow, MD, director of the National Institute on Drug Abuse, about the strong link between opioid use disorders and suicidal thoughts and behavior Furthermore, a 2004 literature review on substance use disorders and suicide found that individuals with opioid use disorders had a 13 times greater risk of completed suicide, compared with the general population.¹²
- A recent study of nearly 5 million veterans enrolled in the Veterans Health Administration demonstrated that, even when adjusted for age and comorbid psychiatric diagnoses, opioid use disorder was associated with an increased risk for suicide; particularly striking was that this risk was doubled in women
- A survey of 40,000 subjects from the 2014 National Survey on Drug Use and Health demonstrated that prescription opioid misuse was associated with an increased risk of suicidal ideation, and weekly misuse was associated with increased suicide planning and attempts.



Genesis of Global Toxic Adulterant Project

- In 2010, Brazil treatment centers at a national conference asked INL for assistance in finding the cause of unusual infections, diseases, and health problems among cocaine-using clients
- INL contacted Brazil Federal Police (DPF) National Institute of Criminalistics drug testing lab for information on composition of cocaine samples seized throughout Brazil
- DPF chemists had analyzed thousands of cocaine samples (HCl & Crack) and published numerous articles on cocaine composition in peer-reviewed journals
- Data showed that aminopyrine, phenacetin, and levamisole were new toxic adulterants being added to cocaine since 2010
- Adulterants which reduced white blood cells (aminopyrine & levamisole) explained infections & diseases due to compromised immune systems and adulterants associated with renal failure (phenacetin) explained kidney problems.

Chemical Profile of Cocaine Samples – Brazil 2012



Chemical Profile of Cocaine Samples Southern Cone - 2012

	Brazil	Chile	Paraguay	Uruguay	Argentina
No. Samples Tested:	40	20	20	9	15
Average Purity (Range)	(29.7% -89.6%)	(15.8% - 92.2%)	(4.6% – 84.6%)	(35.8% - 82.4%)	(17.4% - 18.4%)
Number (%) with Adulterants	30 (75%)	8 (40%)	17 (85%)	9 (100%)	15 (100%)
Phenacetin	26 (65%)	1 (5%)	13 (65%)	2 (22%)	15 (100%)
Levamisole	1 (3%)		1 (5%)	2 (22%)	
Other	3 (7%)	7 (35%)	3 (15%)	5 (55%)	
Aminopyrine + Phenacetin	16 (40%)	-	8 (40%)	1 (11%)	

Chemical Profile of Cocaine Samples in Sao Paulo – Nov. 2014 (1144 samples)

Adulterants	Crack	HCl
Phenacetin	60%	6%
Aminopyrine	25%	1%
Levamisole	1%	50%

Severe Health Problems Accelerated with Adulterated Drugs versus Adulterated Aspirin

Health Problems from Aspirin Containing Phenacetin Took Years to Appear. Aspirin was Taken as needed for Pain in the 1960s



**Crack Used 15 X day X 7 days/week X 6 months
Today Health Problems Appear within Months**



Global Expansion of Toxic Adulterant Project

- In 2015, INL received reports of toxic adulterant expansion throughout the Andean and Southern Cone regions of South America
- Reporting also indicated that adulterants were spreading along the cocaine trafficking route from South America to Africa and Asia
- INL expanded the project in late 2015 to test street and wholesale drugs for toxic adulterants on a global basis in collaboration with the Colombo Plan
- Project planning visits were taken to Argentina (Feb 2016) & Brazil (Mar 2016)

April 2016 Drug Adulterant Testing Results

Peru

PCB (cocaine paste base): 1 combo

1. Phenacetin

May 2016 Drug Adulterant Testing Results

Argentina

Paco (cocaine paste base): 2
combos

1. Phenacetin and Metamizole
2. Phenacetin and Aminopyrine

Ecuador

2 new street drugs called “H”

1. Heroin cut with diltiazem, phenacetin, and cocaine
2. Heroin cut with aminopyrine, diltiazem, tolycaine, noxiptiline diethyl phthalate

Cocaine HCl

-- cut with levamisole and lidocaine

Chemical Profile of Wholesale Drug Samples in South Africa – May 2017 (50 samples each)

Adulterants	Cocaine	Heroin
Phenacetin	94%	32%
Acetaminophen	--	18%
Levamisole	16%	--

Toxic Adulterants Detected in Africa & Asia: 2016 - 2017

Adulterant	Classification	Country Detected	Health Consequences	Street Drug
Diethyl Methylphosphonate	Nerve Agent (precursor Sarin & Somon gas) Flame Retardant	South Africa (Pretoria) [June 2016]	*Respiratory failure *Convulsions *Paralysis	Pink tablets sold as gym morphine
Maneb	Fungicide Neurotoxin	South Africa (Johannesburg) [June 2016]	*Parkinson's symptoms *Tremors *Muscle rigidity/Slow gait *Impaired voice/Jaw stiffness	Sold as new street drug called 'Swipe' by mixing maneb, corn syrup & talc powder
Nitroethane	Neurotoxin	South Africa (Johannesburg) [June 2016]	*Genetic damage *Harmful to nervous system, liver, and kidneys	Used to cut <i>nyaope</i> or <i>whoonga</i> (a heroin concoction with several adulterants)
Chinomethionate	Fungicide Neurotoxin Carcinogen		----- --- *Causes cancer *Damage to bodily organs	
Di(ethylene glycon) dibenzoate	Neurotoxin Industrial Solvent	South Africa (Cape Town) [June 2016]	*CNS Depression *Neurologic dysfunction *Liver/Kidney damage	Used to cut crack cocaine (also adulterated with phenacetin)
2,2diethoxyacetophenone	Carcinogens	Thailand (Bangkok) [April 2017]	*Causes Cancer	Used to cut cocaine HCl
Methyl benzoyl formate			*Organ toxicity – single exposure *Skin corrosion/irritation *Respiratory tract irritation	

August 2017 Drug Adulterant Testing Results

- Drug Testing in **Tegucigalpa, Honduras** detected *Levamisole* Levels in Cocaine HCL samples between **60 – 80 %**
- Honduras is a Transit Country for U.S. Bound Cocaine
- *Levamisole* levels in U.S. Cocaine HCl samples were **13%** in July 2014*

*DEA Cocaine Signature Program Report. July 2014.

Health Consequences of Adulterants

Adulterant	Classification	Country Detected	Health Consequences	Street Drug
Phenacetin	Analgesic	United States, Ecuador, Argentina, Peru, South Africa, Brazil	<ul style="list-style-type: none"> *Hemolytic anemia (reduction red blood cells) *Kidney Failure *Bladder Cancer *Analgesic Nephropathy 	Heroin, "H," Coca Paste, Paco, Cocaine HCl, Crack
Levamisole	Medication used for expelling worms	United States, Ecuador, Argentina, Brazil, South Africa, Sri Lanka, Honduras	<ul style="list-style-type: none"> *Fever *Agranulocytosis (reduction white blood cells) 	Cocaine HCl, Heroin, Methamphetamine
Lidocaine	Local Anesthetic	United States, Ecuador, Brazil, South Africa	<ul style="list-style-type: none"> *CNS Problems *Nausea *Vomiting *Dizziness *Tremors *Convulsions *Arrhythmia 	Cocaine HCl, Heroin
Benzocaine	Local Anesthetic	United States, South Africa, Brazil	<ul style="list-style-type: none"> *Blood disorder (Methemoglobinemia: inability to release oxygen effectively to body tissues) 	Crack, Heroin
Aminopyrine	Analgesic Anti-inflammatory	United States, Argentina, Brazil	<ul style="list-style-type: none"> *Agranulocytosis (reduction white blood cells) 	Crack, Paco, Heroin

Health Consequences of Adulterants

Adulterant	Classification	Country Detected	Health Consequences	Street Drug
Diltiazem	Calcium channel blocker Antihypertensive drug	United States, Ecuador	<ul style="list-style-type: none"> *Heroin laced with Diltiazem could cause users to overdose *Bradycardia *Hypotension 	Heroin, "H"
Metamizole/Dipyrone	Pain killer Fever reliever Spasm reliever	United States, Argentina	<ul style="list-style-type: none"> *Agranulocytosis (reduction white blood cells) *Aplastic anemia 	Heroin, Paco
Acetaminophen	Analgesic	United States, South Africa, Afghanistan,	<ul style="list-style-type: none"> *With heroin, dramatically depresses heart rate and breathing *Acute liver (hepatic) failure *Coma 	Heroin, Cocaine HCl
Diphenhydramine	Antihistamine	United States	<ul style="list-style-type: none"> *With heroin, dramatically depresses heart rate and breathing *Tachycardia *Torsade de Pointes *Encephalitis *Seizures 	Heroin, Cocaine HCl, Methamphetamine
Caffeine	Psychoactive Stimulant	United States, Argentina, Brazil, Peru, Ecuador, South Africa, Thailand	<ul style="list-style-type: none"> *Neurodegenerative disease *Respiratory distress *Arrhythmia 	Heroin, Cocaine HCl, Paco, "H," Methamphetamine, Coca Paste

Health Consequences of Adulterants

Adulterant	Classification	Country Detected	Health Consequences	Street Drug
Xylazine	Veterinary Anesthetic Muscle relaxant Analgesic Sedative	United States	<ul style="list-style-type: none"> *Respiratory depression *CNS depression *Bradycardia *Hypotension 	Heroin
Tramadol	Opioid pain medication	United States	<ul style="list-style-type: none"> *Respiratory distress and death when taken in high doses or when combined with other substances *Serotonin syndrome *Seizures *Convulsion at high doses 	Heroin
Carisoprodol	Muscle Relaxant	United States	<ul style="list-style-type: none"> *Potentiating effect on narcotics *CNS & respiratory depression *Dangerous when combined with other sedatives or alcohol 	Heroin
Quetiapine	Antipsychotic for major depressive disorder, bipolar disorder, and schizophrenia	United States	<ul style="list-style-type: none"> *Torsade de Pointes *Respiratory failure *Tachycardia *Neutropenia *Hypotension *Sudden cardiac arrest 	Heroin

Health Consequences of Adulterants

Adulterant	Classification	Country Detected	Health Consequences	Street Drug
Alprazolam	Benzodiazepine	United States	<ul style="list-style-type: none"> *CNS depression *Hypotension *with opioids & alcohol, may cause profound sedation, respiratory depression, coma, and death 	Heroin
Quinine	Antimalarial Medication	United States	<ul style="list-style-type: none"> *Kidney damage *Arrhythmias *Brown-Sequard syndrome *Cardiovascular toxicity *Torsade de Pointes *CNS overstimulation *Thrombosis *Hypotension *Acute renal failure 	Heroin, Cocaine HCl
Procaine	Local Anesthetic	United States	<ul style="list-style-type: none"> *CNS problems *Convulsions *Poisoning at high doses 	Heroin, Cocaine HCl

Health Consequences Illicitly Manufactured Heroin Impurities

- Acetylcodeine – **potentiates the convulsant effects of heroin** suggesting a mechanism for some of the heroin-related deaths reported in human addicts.
- 6-Monoacetylmorphine (6-MAM) - **Thirty (30) percent more active than heroin**. Can cause **CNS depression**.
- Papaverine - comprises 0.5 to 2.5% of opium. **Lowers blood pressure**. Can cause **CNS depression**.
- Noscapine - comprises 4 to 8% of opium. **Toxic at high doses**. Side effects include **increased heart rate**.
- Morphine - unreacted morphine is present in poorly processed heroin. Can cause **neurodegeneration** (loss of nerve structure and function). Can cause **respiratory distress** and **death** when taken in high doses or combined with other substances, including alcohol.
- Codeine - unreacted codeine is present in some poorly processed heroin. Can cause **CNS depression**. Can cause **respiratory distress** and **death** when taken in high doses or combined with other substances, including alcohol.

Expansion of Toxic Adulterant Project to the U.S. (2017)

- Realizing that the same source countries for Latin America, Asia, and Africa also supplied the United States with drugs, Colombo teamed with JMJ Technologies and NMS Labs to test U.S. street-level drug samples for the same toxic adulterants detected worldwide
- NMS Labs obtained over 500 street-level drug samples from state-level drug testing labs in Vermont and Kentucky
- Analysis showed that opioids, cocaine, and other drugs are adulterated with multiple, highly toxic adulterants like other countries worldwide
- Results of this analysis indicated a **'hidden' adulterant epidemic** that adds a new, unforeseen dimension to the U.S. opioid overdose crisis

- The general narrative today is that fentanyl-laced heroin and overprescribing of opioid pain medicines are driving the nation's opioid overdose epidemic.
- This narrative “fails to capture the full dimensions of the problem and leads to inadequate and even confounding solutions.” *
- The current drug problem is far more complex.

*DuPont, R.L. (2017). The opioid epidemic is an historic opportunity to improve both prevention and treatment. *Brain Research Bulletin*, pii:S0361-9230(17), 3092-3097.

- A recent CDC study found that fentanyl was detected in only half of serum samples drawn from patients who died from opioid overdose deaths in multiple states between July – December 2016*.
- Thus, fentanyl is undoubtedly contributing to overdose rates, but it is far from their only cause.

*O'Donnell JK, Halpin J, Mattson CL, Goldberger BA, Gladden RM. Deaths Involving Fentanyl, Fentanyl Analogs, and U-47700 — 10 States, July–December 2016. MMWR Morb Mortal Wkly Rep 2017;66:1197–1202. DOI: <http://dx.doi.org/10.15585/mmwr.mm6643e1>

Opioids and other drugs are now increasingly cut with multiple, highly toxic substances, in some cases as many as **ten (10)** adulterants, other controlled drugs, and impurities from the heroin manufacturing process, in addition to fentanyl.

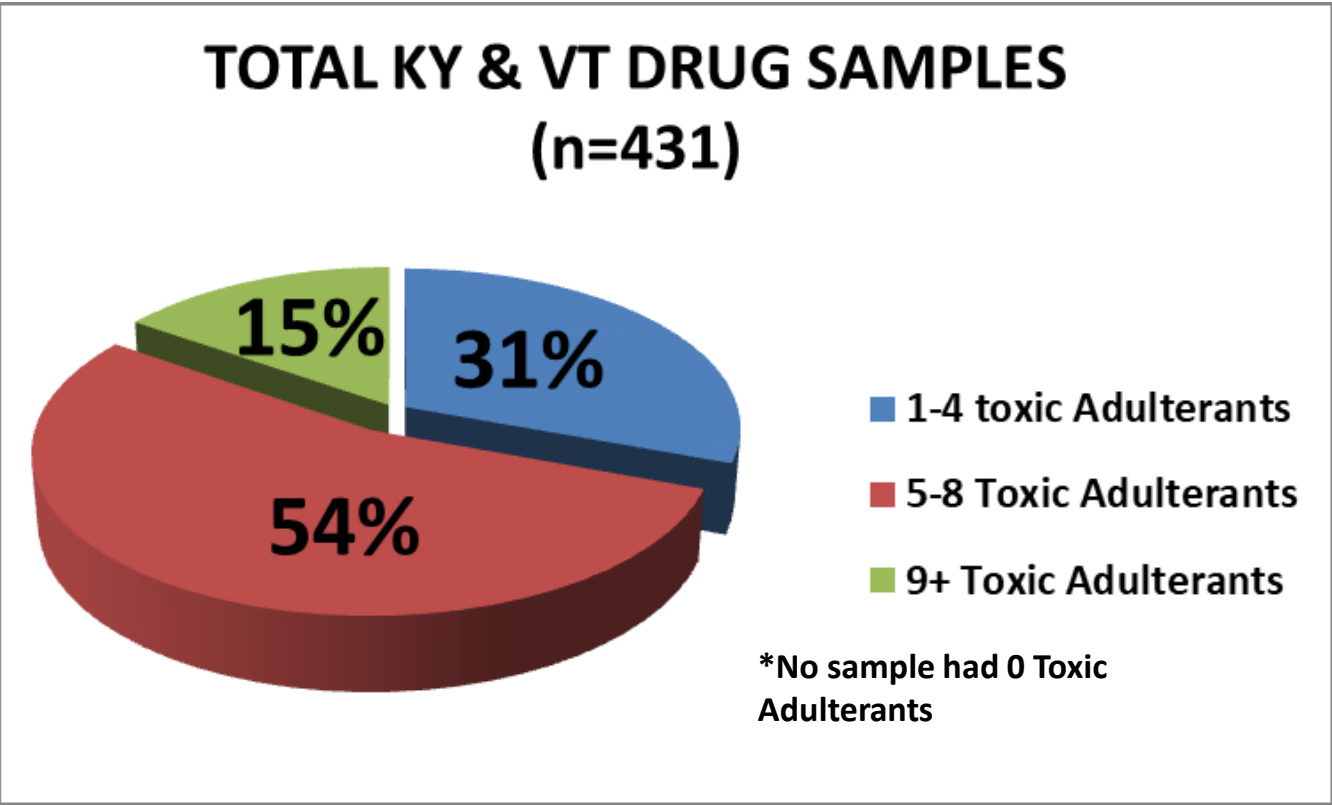
U.S. drug samples analysis shows that fentanyl was not the only toxic adulterant in seized materials tested by Quadrupole Time of Flight (QTOF) Mass Spectroscopy, a technology not routinely available in analysis of seized materials or biological samples.

This novel U.S. data suggest that absent fentanyl, overdose and severe near-term health problems, even death, could occur due to a **synergistic and poisonous effect of multiple toxic adulterants, other controlled substances, and heroin impurities now routinely added to street drugs.**

**In 2017 the Colombo Plan project tested
431 U.S. opioid and cocaine street drug samples
from Vermont (VT) and Kentucky (KY) for adulterants.**

- QTOF analyses of the samples by the National Medical Laboratories (NMS) in Pennsylvania identified numerous controlled substances, toxic adulterants, and impurities from the heroin manufacturing process in a majority of samples.
- Five **(5)** or more substances **(69%)**, with or without fentanyl, were found in **VT** and **KY** samples.
- Nine **(9)** or more substances **(15%)**, with or without fentanyl, were found in **VT** and **KY** samples.
- Adulterants included phenacetin, levamisole, aminopyrine, dipyrrone/metamizole, diltiazem, xylazine, carisoprodol, alprazolam, modafinil, quinine, diphenhydramine, lidocaine, and others.

Vermont & Kentucky Street-level Drug Samples (2016 - 2017)



Vermont & Kentucky Street-level Drug Samples (2016 - 2017)

VT #156	VT #160	KY #26	KY #105
Heroin	Heroin	Heroin	Heroin
Cocaine	Cocaine	Cocaine	Cocaine
Tramadol	Fentanyl	Tramadol	Fentanyl
Ketamine	Levamisole	Fentanyl	4-ANPP
Fentanyl	Acetaminophen	4-ANPP	Acetaminophen
Aminopyrine	Quinine	Aminopyrine	Diphenhydramine
Diltiazem	Lidocaine	Diphenhydramine	Levamisole
Quinine	Procaine	Quinine	Phenacetin
Quetiapine	Caffeine	Lidocaine	Quinine
Caffeine	Acetylcodeine	Dipyron	Caffeine
Acetylcodeine	6-MAM	Caffeine	Acetylcodeine
6-MAM	Papaverine	Acetylcodeine	6-MAM
Noscapine	Noscapine	6-MAM	Papaverine
Papaverine		Papaverine	Noscapine
Morphine		Noscapine	

Legend:

Black = controlled drugs

Purple = fentanyls

Red = adulterants

Green = impurities from heroin manufacturing process

Kentucky Heroin Samples Containing Fentanyl

KY26	Fayette	4/4/2017	Caffeine (0.73, 39687) Diphenhydramine (2.04, 723315) Lidocaine (0.63, 33334) Aminopyrine (0.63, 3296) Tramadol (0.78, 4107) Cocaine (1.07, 1923) 4-ANPP (1.96, 11284) Acetylcodeine (0.71, 5834) 6-MAM (0.56, 881) Heroin (0.72, 100970) Fentanyl (1.99, 494025) Quinine/Quinidine (0.84, 21406) Papaverine (1.5, 7189) Noscapine (1.6, 757897) Dipyrone Breakdown Products
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Kentucky Heroin Samples Containing Fentanyl

KY75	Fayette	4/11/2017	Acetaminophen (0.56, 122989) Caffeine (0.6, 188443) Diphenhydramine (2.05, 483398) Lidocaine (0.69, 15537) Tramadol (0.92, 13238) Cocaine (1.22, 9010) Acetylcodeine (0.88, 8402) 6-MAM (0.57, 4347) Heroin (0.92, 193539) Fentanyl (2.01, 351398) Quinine/Quinidine (0.98, 432958) Noscapine (1.71, 63441)
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Kentucky Heroin Samples Containing Fentanyl

KY103	Fayette	5/2/2017	Acetaminophen (0.56, 202305) Diphenhydramine (2.05, 653847) Cocaine (1.18, 14721) Quinine/Quinidine (0.92, 1026216) 6-MAM (0.57, 5553) Fentanyl (2, 6885) Heroin (0.82, 1334068) Noscapine (1.7, 559691) Phenacetin (1.84, 4080) Acetylcodeine (0.79, 33227) Caffeine (0.6, 345509) Papaverine (1.61, 15316)
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Kentucky Heroin Samples Containing Fentanyl

KY113	Fayette	5/2/2017	Diphenhydramine (2.05, 573324) Cocaine (1.25, 5639) Quinine/Quinidine (1.01, 12070) 6-MAM (0.56, 9545) Fentanyl (2, 201752) Papaverine (1.67, 8713) Heroin (0.95, 747463) Noscapine (1.73, 204490) Acetylcodeine (0.9, 32648) Caffeine (0.61, 4280) 4-acetylaminoantipyrine Dipyron BP (0.68, 3277) Aminopyrine (0.56, 1517)
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Kentucky Heroin Samples without Fentanyl

KY159	Jessamine	5/3/2017	Acetaminophen (0.55, 50242) Caffeine (0.59, 105451) Diphenhydramine (2.04, 225665) Cocaine (1.11, 11312) Quinine/Quinidine (0.88, 421766) 6-MAM (0.56, 12828) Papaverine (1.55, 21837) Heroin (0.17, 958644) Noscapine (1.64, 334002) Acetylcodeine (0.73, 23106) Methamphetamine (0.57, 10477) Amphetamine (0.58, 23824)
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Vermont Heroin Samples Containing Fentanyl

VT23	Drug Task Force	4/29/2016	Acetaminophen (0.55, 1288) Caffeine (0.57, 3880) Ketamine (0.6, 465191) Cocaine (1.01, 1969) Codeine (0.59, 116) Morphine (0.55, 447) Acetylcodeine (0.67, 21568) 6-MAM (0.56, 12100) Heroin (0.68, 994268) Fentanyl (1.97, 9491) Quinine/Quinidine (0.76, 31525) Papaverine (1.42, 27708) Noscapine (1.53, 30650) Diltiazem (2.11, 7674)
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Vermont Heroin Samples Containing Fentanyl

VT105	Orleans	3/10/2017	Caffeine (0.6, 19825) Diphenhydramine (2.03, 1287) Levamisole (0.56, 7049) Tramadol (0.9, 4416) Cocaine (1.19, 16485) Codeine (0.56, 271) Morphine (0.55, 711) Acetylcodeine (0.84, 29375) 6-MAM (0.56, 36908) Heroin (0.89, 1036044) Fentanyl (1.99, 229619) Papaverine (1.6, 11515) Noscapine (1.68, 42670)
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Vermont Heroin Samples Containing Fentanyl

VT150	Windsor	2/2/2017	Caffeine (0.6, 442400) Aminopyrine (0.56, 254713) Tramadol (0.84, 281569) Morphine (0.56, 56) Acetylcodeine (0.76, 12423) 6-MAM (0.55, 2421) Heroin (0.78, 237471) Fentanyl (1.99, 163814) Quinine/Quinidine (0.88, 182947) Noscapine (1.64, 1187745) Quetiapine (2.06, 555857) Ketamine (0.63, 3215) Papaverine (1.55, 10128) Diltiazem (2.12, 43384)
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Vermont Heroin Samples Containing Fentanyl

VT315	Drug Task Force	1/30/2017	<p>Lidocaine (0.65, 317389)</p> <p>Quinine/Quinidine (0.9, 104901)</p> <p>Fentanyl (1.99, 225959)</p> <p>Heroin (0.8, 246684)</p> <p>Diltiazem (2.12, 77861)</p> <p>Procaine (0.56, 103698)</p> <p>4-acetylaminoantipyrine - Dipyron BP (0.61, 11351)</p> <p>Acetylcodeine (0.77, 10966)</p> <p>6-MAM (0.57, 866)</p> <p>Aminopyrine (0.58, 747)</p>
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Vermont Heroin Samples without Fentanyl

VT36	Drug Task Force	4/29/2016	Acetamoniphen (0.56, 10781) Caffeine (0.6, 8458) Methocarbamol (1.23, 261) Procaine (0.57, 175) Morphine (0.56, small peak) Acetylcodeine (0.83, 16754) 6-MAM (0.56, 12570) Heroin (0.86, 455575) Quinine/Quinidine (0.9, 206359) Papaverine (1.58, 8740) Diltiazem (2.11, 8368) Noscapine (1.66, 114581) Quetiapine (2.05, 463)
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- The VT and KY adulterants include, but are not limited to, **banned pharmaceuticals, veterinary products, analgesic pain relievers, sedatives, antihistamines, opioid pain medications, muscle relaxants, antiarrhythmics, and impurities from the heroin manufacturing process.**
- These compounds have been associated with severe health effects, including **decreased production of red and white blood cells due to bone marrow damage, multifocal inflammatory leukoencephalopathy, hemolytic uremic syndrome, renal failure, multiple malignancies, and life-threatening cardiac arrhythmias.***
- Variation in the substances used to adulterate street drugs and their concentrations contributes to the unpredictability of the drug's effects, and the potential for unknown, unexpected, and potentially life-threatening effects.**

*Mark Gold. Deadly Adulterants: New Dangers of Illicit Drugs. The Sober World Magazine – July 2017.

*Phillips et al. Cardiac complications of unwitting co-injection of quinine/quinidine with heroin in an intravenous drug user. J Gen Intern Med 27(12): 1722-5.

**Cole et al. Adulterants in illicit drugs: a review of empirical evidence. Drug Testing Analysis 2011, 3, 89 – 96.

- This drug testing data corresponds with post-mortem data reported by the Florida Drug-Related Outcomes Surveillance and Tracking System (FROST) at the University of Florida.
 - In 2017, over 90% of opioid overdose deaths in the state of Florida included other, non-opioid, drugs. An average of 2-3 non-opioid drugs have been identified in the serum of patients who died due to opioid overdoses.*
 - Some individuals had as many as 11 additional drugs present in their system at the time of autopsy.*
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*DuPont, R.L. (2017). The opioid epidemic is an historic opportunity to improve both prevention and treatment. Brain Research Bulletin, pii:S0361-9230(17), 3092-3097.

*University of Florida College of Medicine, 2017. Florida Drug-Related Outcomes Surveillance and Tracking System (FROST). University of Florida. [updated 2017; cited May 2017]; Available from: <http://frost.med.ufl.edu/>.

These Data Corresponds with DEA Heroin Signature Program and DEA Heroin Domestic Monitor Program

- In 2014, the majority of **South American-origin heroin** in the U.S. contained significant adulteration, such as **diltiazem, phenacetin, caffeine, procaine, aminopyrine, quinine, lidocaine, acetaminophen, diphenhydramine, and xylazine**;^{*}
- while **Mexican-origin heroin** contained **lidocaine, diphenhydramine, and caffeine**.^{*}
- In 2015, **South American-origin heroin** samples routinely contained **diltiazem, lidocaine, quinine, benzocaine, acetaminophen, caffeine, and diphenhydramine**;^{**}
- while **Mexican-origin heroin** contained **quinine, lidocaine, acetaminophen, diphenhydramine, and caffeine**.^{**}

^{*}DEA Intelligence Report. The Heroin Signature Program and Heroin Domestic Monitor Program 2014 Reports. DEA-DCW-DIR-051-16. September 2016.

^{**}DEA Intelligence Report. The 2015 Heroin Signature Program Report. DEA-DCW-DIR-032-17. August 2017.

^{**}DEA Intelligence Report. 2015 Heroin Domestic Monitor Program. DEA-DCW-DIR-035-17. October 2017.

These toxic adulterants and impurities can cause numerous medical consequences including death.

Unfortunately, these substances are not routinely tested by forensic laboratories on seized materials or in clients undergoing substance use treatment.

Failure to identify these “**hidden**” toxic adulterants can hinder accurate clinical diagnosis and the development of appropriate treatment plans in addicts exposed to these poisons, in addition to misclassification of drug epidemics.

What effects do adulterants have on *Naloxone*, an opioid antagonist designed to rapidly reverse opioid overdose?

- Naloxone only partially reverses the toxic effects of Tramadol overdose and may increase the risk of seizures.*
- Naloxone will not reverse overdose resulting from non-opioid drugs, like benzodiazepines (e.g., alprazolam).**
- The effects of multiple toxic adulterants, controlled drugs, and impurities from the heroin manufacturing process in individual drug samples on Naloxone are unknown, as are the synergistic and poisonous effects of these drug combinations on the user.

*Rossi, S, ed. (2013). Australian Medicines Handbook (2013 ed.). Adelaide: The Australian Medicines Handbook Unit Trust. ISBN 978-0-9805790-9-3.

**Bureau of Justice Assistance. Law Enforcement Naloxone Toolkit. BJA National Training and Technical Assistance Center.

Recommendations

- Toxic adulterant testing should become a part of standard drug toxicology panels as the process of adulteration is now common and the synergistic effects of multiple adulterants are unknown
- Testing would help promote public health and safety in community clinics, health care providers, emergency departments, medical examiners, crime laboratories, and substance abuse treatment centers
- Expanded adulterant testing and reporting is needed to identify emerging drug/adulterant trends
- Targeted public health alerts are needed in communities and jurisdictions where toxic adulterants have been identified in street drugs to improve public health response
- Additional research to better understand patterns of toxic adulterant addition to street drugs and potential contribution to morbidity and mortality.
- A comprehensive *Toxic Adulterants Health Risk Assessment* that identifies the interactive effects of multiple controlled drugs, toxic adulterants, and heroin impurities found in individual street drug samples to better guide clinical and medical practice.

Heroin & Other Illicit Drugs Track

America's Hidden Drug Epidemic: It's More than Opioids

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