STAMPS: SURVEILLANCE, TRENDS AND MAPPING OF OPIOID SEIZURES: ALLEGHENY COUNTY, PENNSYLVANIA

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Submitted to the Graduate Faculty of

the Department of Epidemiology

Graduate School of Public Health in partial fulfillment

of the requirements for the degree of

Doctor of Public Health

University of Pittsburgh

2018

UNIVERSITY OF PITTSBURGH

Graduate School of Public Health

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ABSTRACT

The rapid rise of heroin and fentanyl over the past few years has become a troubling and overwhelming public health issue. Mortality from drug-related overdose has surpassed other historically leading causes of death, such as unintentional motor-vehicle accidents. Heroin and non-prescription fentanyl have become associated with increases in opioid mortality, particularly in the Northeastern United States. However, epidemiologic studies and standard surveillance data systems do not adequately capture different combinations of illicit drugs and emerging drug threats. Stamp bags, which are small wax packets typically used to sell heroin, are one type of drug evidence that can be used to evaluate drug patterns on the street.

The purpose of this dissertation is to utilize a stamp bag dataset to examine trends in illegal drugs in Allegheny County, Pennsylvania. Specifically, we aim to build and describe a database of stamp bag information from 2010 through 2017, evaluate geographic trends in illegal drugs across the county and over time, and describe the rapid rise in illicit fentanyl and emerging synthetic drugs using these data.

Public Health Significance: the dataset we are using is a departure from traditional measures in public health with a focus on the rapid rise of illicit fentanyl. Stamp bag data has not been used to evaluate public health problems as compared to morbidity and mortality data. In public health peer-reviewed literature, this data has not been described or used to evaluate patterns in illegal drug supply.

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PREFACE

This work would not have been possible without the collaboration and expertise of individuals at the Allegheny County Medical Examiner's Office, including Dr. Karl Williams and Joshua Yohannan. I would also like to thank my mentors, dissertation committee members and collaborators on this project including Dr. Anthony Fabio, Dr. Steve Wisniewski, Dr. Jeanine Buchanich, Dr. Thomas Songer, Dr. Christina Mair, Dr. Nancy Glynn and Dean Donald Burke.

This study was completed with the data use agreement DUA00000648and approved by the University of Pittsburgh Institutional Review Board PRO16090161.

For Mom, Dad, Lauren, Evan, Chris, Killian, Chase and Caroline, and all my friends and family who have been supportive for my extensive educational journey, one that I am sure will continue for the rest of my life

1.0 INTRODUCTION

"Each day, 46 people die from an overdose of prescription painkillers in the US." (1)

In 2017, CDC published a report with troubling statistics; using medical claims data, it is estimated that a single day prescription increases the risk of continued abuse or dependency by 6%. (2). Given this information, it is perhaps even more important to recognize that 20% of patients with pain (unrelated to cancer) will receive an opioid prescription. (3) This serves as a reminder that the opioid epidemic continues into the present day, even with changing trends among prescribing, drug use, and illicit drugs. With drug-related overdose death remaining the leading cause of unintentional injury death in the United States (4) and nonfatal overdoses increasing six-fold since the late nineties (5), future research and surveillance of drug overdose will be critical to ascertain the burden of disease and death, develop more effective prevention strategies, and pinpoint continuing problematic risk factors that precipitate drug misuse and abuse. Still, almost 30% of the United States does have legitimate chronic pain that warrants some sort of treatment. (5)

In Pennsylvania, this upward trend in drug-related overdose mortality has been even more pronounced as compared to the rest of the United States. (6; 7) Middle aged white males are particularly affected (6).

Apart from legally prescribed opioids, there has been a surge in heroin (8; 9), and illicit fentanyl-related overdose where heroin is mixed with fentanyl. (9) This is an escalating issue that requires attention and concern by the public health community and its stakeholders. Since these drugs are highly addictive and adulterated heroin has the potential to be highly lethal, there is reason to expect this trend to continue over time as illicitly manufactured fentanyl continues to be mixed with heroin. (10; 11)

1.1.1 Overall Objectives and Aims

This dissertation is part of an applied track in Epidemiology and in pursuit of a DrPH at the University of Pittsburgh Graduate School of Public Health. The purpose of this manuscript is to utilize a non-traditional dataset for public health surveillance and to examine the changing landscape of illicit opioids in Allegheny County, Pennsylvania. Part of the data consists of laboratory drug chemistry results of tested stamp bags in the county, which are small, wax packets that are used to contain and sell heroin. The second part of the data consists of matching law enforcement records that describe the location of the event where stamp bags were recovered by law enforcement and the individuals present at the scene. *The overall objective is to characterize the trends in illegal drugs (particularly heroin and fentanyl) in Allegheny County, PA from 2010 through 2017 and identify any geographic clustering that may have occurred among combinations of drugs*. Specifically, we aim to:

Aim 1: **Develop an illicit drug surveillance system for use by public health, law enforcement, and the medical examiner by merging data sources from law enforcement and the medical examiner office for incidents of stamp bag seizures**

- Create and standardize drug category definitions for monitoring illicit drugs in stamp bags

- Develop a sustainable infrastructure and process for adding future years of data
- Develop quality control checks for ensuring accuracy of matching, cleaning and measurement
- Create and implement rules for data cleaning, particularly to clean and/or remove duplicate observations and to exclude irrelevant observations
- Describe characteristics of the database, including population characteristics and stamp bag drug contents

Aim 2: Identify spatial patterns among stamp bag seizures in Allegheny County, PA from 2010 through 2017 using the surveillance database

- Geocode addresses using a two-variable matching algorithm to ensure completeness of the data
- Evaluate the burden of stamp-bag related activity among regions across the county using thematic mapping.
- Evaluate the degree of spatial autocorrelation among stamp bag cases using hot spot analysis at the zip code, census tract and block group levels.

Aim 3: Describe the increase in illicitly manufactured fentanyl in Allegheny County, PA using stamp bag data.

- Describe the change in fentanyl that is detected within stamp bags over time, as well as combinations of fentanyl with other drugs
- Identify specific, unique fentanyl analogs that have been detected in the county since 2014

- Report the stamps that are most commonly associated with fentanyl and fentanyl analog stamp bags, as well as the number of unique stamps by year

1.2 THE OPIOID EPIDEMIC

"The amount of opioids prescribed per person was three times higher in 2015 than 1999 (12)

1.2.1 Definitions

Opioids are defined as any substances that have morphine like qualities or effects. They include drugs like oxycodone, hydrocodone, methadone, and heroin. (13; 14) Table 1 displays several commonly prescribed (and abused) drugs along with their class, schedule, and routes of ingestion.(15)

Table 1: List of drugs and corresponding characteristics

Drug	Drug Class	Schedule	Uses	Mechanism of Use
Oxycodone	Semi-synthetic opioid	II	Pain reliever	Snort, inject, eat
Hydrocodone	Semi-synthetic opioid	II	Pain reliever	Snort, inject, eat
Heroin	Semi-synthetic opioid	I	Illegal (in U.S.)	Smoke, snort, inject
Methadone	Synthetic opioid	II	Pain relief; maintenance treatment	Inject, eat
Fentanyl	Synthetic opioid	II	Pain reliever	Snort, inject, eat, absorb via patch
Alprazolam	Benzodiazepine	IV	Anxiety and panic	Inject, eat
Buprenorphine	Mixed narcotic agonist/antagonist	III	Pain relief; maintenance treatment	Inject, absorb
Cocaine	Stimulant	II	Illegal	Smoke, inject, rub into gums
Morphine	Opiate	II	Pain relief	Inject, eat, smoke
Marijuana	Cannabinoid	I	Psychoactive	Smoke, eat, drink
Methamphetamines	Stimulant	II	Illegal	Smoke, snort, eat, inject
Tobacco		__	Recreational	Snort, chew, smoke

1.2.2 History

"Enough prescription painkillers were prescribed in 2010 to medicate every American adult around-the-clock for a month." (16)

As noted elsewhere, opium and its derivatives have existed and been used for both therapeutic and illicit purposes for thousands of years. When considering the current epidemic of prescription opioid abuse and overdose, it is critical to reflect on trends and norms in prescribing and clinical practice in the past few decades. Perhaps it is of no surprise that upward trends have been documented in prescription sales (17-18), prescriptions supply (10, 19-20) and prescription use. It has been well-established, though, that there has not been a similar increase in self-reported pain by individuals in the United States (20-21), suggesting that there is indeed a problem and an overall change in how these drugs are being accessed and used, particularly informally shared among friends and family. (22)

1.2.3 Physiology

Opioid overdose occurs when, simplistically, opioid molecules cross the blood-brain barrier and bind to opioid receptors in the brain. (23) Heroin overdose occurs via similar mechanism; that is, it is metabolized to morphine and binds to opioid receptors in the brain. In the case of heroin, this process occurs very rapidly and results in a quick feeling of euphoria. Thus, the individual's breathing is depressed. (24) Much like an opioid overdose, heroin-related overdoses can be reversed with the timely administration of naloxone. (25)

1.2.4 Epidemiology

Non-fatal overdose, abuse and misuse of opioids has been documented at the local, state and federal level among all age groups. Between 1993 to 2012, hospitalizations related to opioid misuse or overdose among adults increased by 150% (26). Starting in 2001, there were roughly 663,715 opioid and heroin-related hospital admissions up until 2012, representing yet another slight increase in hospital visits for overdose. (27) For adults, these increases were fueled by user groups that typically had lower rates of abuse or misuse such as women or very elderly individuals. (26, 28) Heroin users, as expected, were younger than individual who visited with opioid-related issues. (27-28)

Each day, hundreds of individuals in the United States visit the emergency department for opioid misuse or abuse. (29) Specifically, visits for non-medical use of opioids, particularly oxycodone, increased by 111% between 2004 and 2008. (30) A systematic review evaluated the lifetime prevalence of non-fatal overdose worldwide and found rates as low as 16% and as high as 68%. (31) Hospitalizations, regardless of where they occur, are also extremely costly to the healthcare system, (32) with one study estimating $700 million in annual hospital costs. (27)

Prescription drug abuse has also become an alarming issue among adolescents and young adults. Among younger individuals, the prevalence of self-reported narcotic use among 12th graders were 4.8% in 2016. In 2015, the past-year self-reported prevalence of narcotics use among individuals ages 18 to 25 was 8.5% and 0.6% for heroin. (13).

1.2.5 Risk Factors for Overdose

The opioid epidemic is strikingly different in terms of who is at greatest risk of overdose, misuse and abuse. Individuals with the highest risk are white, middle-aged males (33-34). Geographically, drug misuse and abuse are no longer restricted by urbanicity; rural areas, including Appalachia and the rural South, have tremendous rates of overdose and fatal overdose (18, 35, 36) However, no one person or area is immune from this epidemic. In fact, some of the demographics of opioid users and the subsequent risk factors for overdose have changed as the epidemic has progressed.

Women, as a risk group, are more likely to be prescribed these painkillers and tend to have more chronic and acute pain than men. (28, 37, 38) White women are five times more likely to receive prescriptions for both opioids and benzodiazepines than their male counterparts, which is also a major risk factor for overdose (39, 40) and consequently, the increase in the rate of opioid-related overdose mortality has been larger for women than for men in the past decade. (37)

1.2.6 Mortality

"Deaths from prescription painkiller overdoses among women have increased more than 400% since 1999, compared to 265% among men." (37)

The rate of mortality due to all drug-related overdose surpassed that of motor vehicle traffic accidents for the first time in the past decade (9, 41) and totaled over 165,000 deaths between 1999 and 2014. (3) In 2010, misuse of opioids resulted in 17,000 deaths alone. (40) Figure 1 comes from the National Center for Health Statistics (41) and shows the overdose mortality rate surpassing the motor vehicle mortality rate. Figure 2 displays the rate of overdose deaths involving opioids for the past fourteen years, also from the National Center for Health Statistics. (41) This figure demonstrates the changing trends in opioid-related deaths, particularly with respect to illegal and synthetic opioids (see Figure 2).

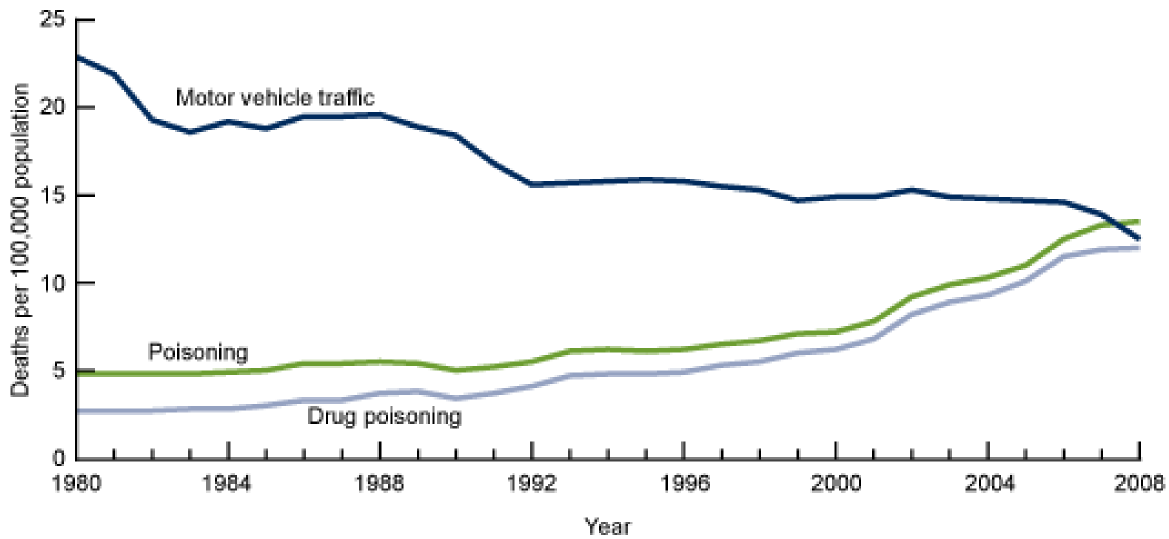

Figure 1: Death Rates by Underlying Cause: Poisoning, Drug-Related and MVC, United States
*Data from the National Center for Health Statistics Brief 81 in 2011.
[1]Poisonings include all poisons. Drug-related includes all drugs and not just opioids.

In 2016, West Virginia had the highest fatal age-adjusted drug-related overdose rate (52.0 per 100,000), followed by Ohio (39.1), New Hampshire (39.0) and Pennsylvania (37.9). Significant increases in mortality occurred in the southern states as well, some by more than 100% (35, 42)

Starting in 2000, the rate of overdose mortality attributed to opioids increased by 200%. (9) Overall, these deaths have increased by more than four times since the nineties, fueled at times by both licit and illicit opioids. (43, 44) Table 2 below displays estimated mortality rates by demographic sub-group for the opioid epidemic from select studies or surveillance reports:

Table 2: Population-based opioid overdose mortality rates for demographic subgroups, all opioids, United States, 2014-2015

Reference Group	Opioid Overdose Mortality Rate	Data Source	Citation
General population	13.3 per 100,000	Vital Statistics	(45)
White	21.1 per 100,000 pop	Vital statistics	(42)
Male	18.3 per 100,000;	Vital statistics	(9)
Middle age (45-54 yrs.)	30 per 100,000 pop	Vital Statistics	(42)
Release from prison; past 2 weeks	1,840 per 100,000	CDC Wonder	(46)

2.0 THE HEROIN EPIDEMIC

"45% of people who used heroin were also addicted to prescription opioid painkillers." (47)

Heroin usage and overdose have increased in recent years during a somewhat declining prescription opioid epidemic. (47-49) In the United States, the death rate from heroin has risen by 20.6% from 2014 to 2015 (9) and tripled between 2010 and 2015. (42). Poison center data suggest that while overdoses due to heroin began to increase in the early 2000's, there was an even larger spike around 2010. (47)

In Pennsylvania, for example, this is an enormous public health problem. From 2015 to 2016, the change in age-adjusted rate of drug overdose fatalities in Pennsylvania was an increase of 44.1%, one of the worst in the nation. (9, 42). Pennsylvania jumped from the 6th highest drug overdose mortality rate in 2015 to the 4th highest in 2016. (9, 42) In Allegheny County, Pennsylvania, nearly 60% of overdose deaths involved heroin (50).

It is important to understand the purity of heroin that enters communities, examine the association with overdose, and identify temporal and geographic trends as demand for heroin increases and new suppliers enter the market. Given limited resources, public health organizations can develop and use alternative methods to identify different types and sources of heroin. Very few, if any, public health entities have utilized stamp bag tracking as a form of surveillance to date. A regional reports of overdose statistics in Kentucky cited "law enforcement submissions" to describe illicit drug evidence. (51) Stamp bags are only one way that heroin is marketed and sold; in the western part of the United States, black tar heroin is transported using balloon-like vehicles (52). Northeastern states, such as New York, Delaware, and Pennsylvania are some of the few regions in the U.S. where stamp bags are widely used. (53) Access to these stamp bags and their drug contents offers a unique opportunity to examine how it might be used for surveillance and prevention of heroin overdose.

2.1.1 History

Drug epidemics, heroin trade, and the concept of "overdosing" is a historical one. (54) Heroin became illegal in the United States in 1920. However, heroin did not make its first appearance in the 20th century. Opium is the parent substance to opiates and opioids, which is derived from dried latex seed capsules of poppy plants (P. *somniferum*). (55). Morphine and codeine are naturally opium-derived substances called alkaloids (56), while heroin is an acetylated derivative of morphine. (57) While opiates such as morphine and heroin are "ancient", other newer opioids have been derived from morphine. Some, like fentanyl and tramadol, are synthetic. (58). As far back as 3400 B.C., the poppy plant was grown and farmed in Mesopotamia (modern day areas in Iraq, Turkey, Syria, Iran and Kuwait) and eventually opium would be extracted from the plant for its pleasurable and medicinal effects. (55, 59, 60) Heroin itself was first manufactured from morphine in 1874 and marketed for therapeutic purposes into the late 1890s. (61).

Historically, opium was cultivated in various warm climates in the Mediterranean and East Asia. (61-63) Currently, the golden crescent of Asia produces and distributes most of opium and heroin worldwide. (55,57) This has ultimately led to an influx of heroin into western nations. In the 1970s the United States put pressure on Turkey to eliminate the drug supply (59) and in

1961 the United Nations convened to restrict the cultivation of opium for legitimate purposes only. (64) Interestingly, there was also political action in the 1960s and 1970s that resulted from fear of widespread heroin addiction after the return of Vietnam veterans. (65-66)

In the seventies and eighties, heroin flowed into New York streets from Southeast Asia, but was gradually replaced with both product and dealers from Mexico and South America. (54, 67) Today, most of the heroin in the United States comes from the Western hemisphere. (67-68) Heroin was considered illegal at this point but flourished on a black market. Historical ethnographic reports for this period mention the “stamp bag” as a common type of drug evidence in the city (54, 69), which could possibly be some of the earliest discussions of stamp bags in the heroin trade.

This brief history of heroin introduces the current heroin epidemic. Heroin can be manufactured in different formulations by different processing methods: white powder from South American and South East Asia (70), brown powder from South West Asia (57), and sticky black tar from Mexico. (52, 70) Each type of heroin is sold in different parts of the United States, with black tar far more prevalent in the Western United States, and white powder in the Eastern United States. (70, 71) While heroin has been in existence for thousands of years, it has ebbed and flowed in terms of its popularity, use, and deadliness.

For the purposes of this dissertation, we will focus on powder heroin that is traditionally found in the Eastern half of the United States and limit the scope to Western Pennsylvania. While the results of these analyses are unique to the specific geographic location and stamp bags included as part of the surveillance “population”, the methodology and lessons learned can be generalized and adapted to other types of drug evidence, other organizations and other geographic locations. However, examining different types of illicit drugs to identify their unique epidemiological characteristics will be important for planning epidemiological studies, interpreting findings, and adapting surveillance for illicit drugs.

2.1.2 Epidemiology of Heroin: Use, Overdose, and Mortality

The rate of overdose deaths from heroin has quadrupled in the past decade from 0.7 to 2.7 per 100,000 between 2002 and 2013. (72-73) In general, this increase has been accompanied by an increase in heroin use and overdose death among all demographic and socioeconomic groups. (72) However, there has been a shift in the demographics of users. (74) Unlike prescription opioid users, most individuals who use heroin or overdose from heroin are young adults. (74-75) This has been made evident by studies of drug use and hospitalization for overdose; in one study, investigators showed that the rate of heroin-related admissions nearly doubled for younger white users between 1993 and 2009. (28) A recent study using nationally-representative NESARC data indicated that increases in heroin use among whites began in the early 2000s. (76). To that point, there has been a ten percent increase in heroin usage among younger white individuals, contrasted with a decline in use among blacks. Similarly, the Unick study demonstrated that heroin-related hospital admission rates for young white users surpassed that of young black users in more recent years (28)

The more recent increases in heroin use were seen among women and individuals with private insurance rather than the previously mentioned high-risk groups, though individuals with prior legal prescription drug use remain at high risk. (47) This has been documented by reported heroin use after initial use of prescription opioids (44,77) The table below lists several select studies that have evaluated the epidemiology of heroin overdose and use. Their estimates and findings are consistent with other literature, and can also be found in the table supporting the general conclusions that this too is an epidemic of white males, albeit slightly younger:

Table 3: Population Based heroin-related mortality rates for 2016 and heroin use rates for select high risk populations, United States, 2008-2011

Group	**Age-Adjusted Rate**	**Data Source**	**Citation**
General population	4.9 per 100,000	Vital Statistics	(78)
White	6.3 per 100,000	Vital Statistics	(78)
Male	7.5 per 100,000 15.5 for ages 25-44	Vital Statistics	(78)
Age: 35-44	9.0 per 100,000	Vital statistics	(78)
Risk Factor	**Self-Reported Past Year Rate, Avg. Annual**	**Data Source**	**Citation**
General population (ages 12 and older)	2.0 per 1000	NSDUH	(44)
Among those with past year cocaine use	95.1 per 1000	NSDUH	(44,74)
Among those with past year nonmed Rx opioids	42.4 per 1000	NSDUH	(44,74)
Males	3.6 per 1000	NSDUH	(47)

2.1.3 Socioeconomic Factors

There have been some ethnographic and epidemiologic studies that examined behavioral and socioeconomic factors that contribute to heroin overdose, or lead to a conducive environment for overdose, including prior nonmedical use of legally prescribed opioids. (25, 54) Most heroin users do not use drugs when they are alone, which serves as a point of intervention to stop overdoses from occurring. (25, 79, 80)

Per Jones et al (2015), heroin *users* that reported past-year heroin use in a national survey were significantly more likely to be uninsured (aOR 3.1; 95% CI 2.2-4.3) or insured through Medicaid (aOR 3.2; 95% CI 1.9-5.4) compared to those with private insurance or alternative forms of insurance. (72) In addition, they were likely to be lower-income. A survey of over 1,300 residents of Baltimore, linked to census data, indicated that residents from poorer neighborhoods in the city were 50% more likely to report using heroin or other illegal drugs (OR=1.51, 95% CI 1.06-21.5) than individuals in wealthier neighborhoods. (81) Elsewhere, both urbanicity and poverty have been shown to be a risk factor for general opiate use. (82-84)

2.1.4 Geographic Distribution

The literature on geographic patterning among heroin users and heroin overdose is inconsistent Historically, urban areas have been dubbed as hot spots for heroin activity (75, 77) and drug activity in general. (85) A study of fatal overdose in Connecticut supported this (75) Urban areas also have higher availability of heroin (86) and heroin mortality rates have shown the greatest increase in metropolitan areas with more than one million people. (78). A recent evaluation of the geographic distribution of heroin and fentanyl-related overdose deaths found that the majority occurred in more populated areas of the state, especially near the Ohio border (51), like past reports in Connecticut. (75) Contrastingly, Paulozzi and Xi (2008) found that there was no detectable difference in urban and rural areas with respect to heroin overdose rates using mortality data. (36) Recently, several studies have looked at differences between rural and urban risk of overdose at the local and national level. Rudd et al. (2014) found significant increases in heroin overdose in the Northeastern, Midwestern and Southern United States. (87)

2.1.5 Changes over Time in Heroin Epidemiology

To summarize, the epidemiology of heroin has changed over time, but inconsistencies remain. A striking comment from a 1974 paper (Greene) was as follows: *"In Washington, D.C., the typical new user was a 17-year old, unmarried, unemployed, black male with a criminal record at the time of onset of heroin use. This picture has been fairly constant across the United States, with the only exception being the racial composition of the user population."* Greene listed rates of heroin use among African American males in Washington, D.C. between 1960 and 1973; in 1969, the rate was 40.4 per 1000 compared to the general population (4.2 per 1000). Findings from a long-term epidemiologic study (77) suggest that the demographics of individuals reporting lifetime heroin use shifted from a younger, mixed male population to an older, white male population in recent years (a finding consistent with the comment above). This finding is also consistent with reports of heroin use across time periods from CDC as well as more recent demographics of fatal heroin overdoses. (88)

While current reports suggest that heroin-related activity falls in more urban areas, there are other anecdotal reports and studies that suggest that heroin is "moving" beyond the cities and into the suburbs. Cerda et al (2013) reported changes in where illegal drug activity was occurring in the most recent decade in New York City, indicating that many of the opioid fatalities were now occurring in higher income neighborhoods within the city. (85)

2.1.6 Illicit Drug Research and the Rise of Fentanyl

Heroin has been sold for decades using pre-stamped bags, a practice that originated in New York City. Branded heroin has a rich history in larger urban areas and has been sold since the early sixties and seventies there. (54) The name "stamp bag" is attributed to the marker, or stamp, that appears on the bag that can be a sign of quality, "brand", or source. In the past it has also been called a dope stamp or dope bag (54, 69). Interestingly, in the past, bags without stamps were less likely to be purchased because there was an air of uncertainty around the product, yet most bags give no indication of purity even with a stamp (54). However, it is difficult to track and analyze stamp bags since the market has such high turnover rates. (89) In the Pittsburgh area, the source of the heroin is identified by the stamp bag (90-91).

Stamp bags contain what is often an unknown concentration and mixture of controlled substances (54, 89), but most commonly heroin. Heroin can be mixed, or "cut", with adulterants and/or diluents to alter the purity and potency of the drug, and therefore change the cost. (67, 92). Evidence from other countries suggests that heroin is cut prior to being sold in the destination country. (93) The purity of heroin in the United States is estimated to be 35% (94).

Adulterants and diluents are not always other drugs; a relatively recent report lists some common non-drug substances that are used substances to cut heroin in the United Kingdom such as caffeine, procaine, mannose, and quinine. (95) Much like the United Kingdom, Mexican and South-American heroin in the United States is cut with lactose, mannitol, quinine, caffeine, and other sugars. (96) Changing trends also occur among adulterants over time. (93) The 2010 report notes that adulterants such as caffeine continue to be present in heroin, while some of the barbiturates and anesthetics have gradually been phased out. (95)

2.1.6.1 Fentanyl: The New Adulterant

Fentanyl has been used as a painkiller for over fifty years in the United States (97), used in the form of a patch, a lollipop, or pills. (98) Fentanyl, unlike heroin, is a legal Schedule II substance with high potential for addiction. It is nearly 20 to 50 times more potent than heroin and 100 times more potent than morphine. (98-99) Fentanyl crosses into the brain quickly and provides a rapid feeling of euphoria, fueling its appeal to habitual drug users but also making it ideal for alleviating acute or post-operative pain (98, 100) Unfortunately, fentanyl has been linked to an increase in opioid-related overdose in the past few years unrelated to its medicinal purposes. In Pennsylvania, there are increasing amounts of fentanyl coming into the state which is contributing to an increase in overdose. (101)

Fentanyl was originally created in the 1960s by a Belgian named Paul Janssen as a newer, more potent opioid painkiller. (102) When clinicians advocated for its use in the United States in the 1960s, there was concern that the drug had major abuse potential given the rapidity and potency it demonstrated. However, fentanyl was eventually incorporated into clinical practice for pain. (102)

2.1.6.2 Synthetic Opioid Mortality

Synthetic opioid overdose deaths (largely fueled by fentanyl) have increased across the United States, but the most dramatic increases have been in the Northeast and Midwest. (87, 103-106) Drug evidence submissions containing fentanyl have also increased in the Northeast and Midwest as compared to the rest of the United States. (103) Exposure to fentanyl-contaminated heroin has also been documented by self-report. (107) When misused, fentanyl has the potential to cause an overdose much more quickly due to its potency. (100, 108-109) Fentanyl can also be accidentally inhaled or absorbed, leaving handlers (such as first responders) at risk of exposure to the drug. (110).

2.1.7 Public Health Significance

According to the most recent report from CDC, the change in national overdose death rates from synthetic opioids and the rate of drug submissions with fentanyl have increased between 2006 and 2015. (103). Heroin-related deaths surpassed the number of deaths from homicides where firearms were used, as well as deaths from drugs such as oxycodone and methadone in 2015. (111). Given that many of these are serious diseases that clearly contribute to significant mortality in the United States, it is important to compare the relative burden of heroin outcomes and confirm the seriousness of this public health problem.

Though much of this will be covered in later chapters, it is important to note that fentanyl is deadly and cheap and can be disguised among other opioids. (108, 112) Acetyl-fentanyl, an analog of fentanyl (112) that has secured media spotlight in the past few years, is equally dangerous in that it is 80 to 100 times more potent than morphine (113) and 5 to 15 times more potent than heroin (114). This fentanyl analog can also be mixed with other drugs, like heroin, reducing the drug purity. (112) A forensic report from Southern Ohio demonstrated that most overdose victims had died because of impure heroin concoctions that were cut with varying concentrations of illicit fentanyl. (115)

2.1.7.1 Pennsylvania: A Local Example

As reported by the DEA, the two most commonly used drugs among overdose fatalities were heroin and fentanyl in 2015. (116). In Western Pennsylvania, the numbers are alarming. In

Allegheny County, a western county in Pennsylvania near the Ohio border, most fatal overdose victims in the county had heroin in their system (51.0%), followed by alcohol (33.0%), cocaine (32.0%) and fentanyl (33.0%) between 2008 and 2017. It is important to note that these are not mutually exclusive, and most individuals who overdose die from multiple drug toxicity (50) Heroin has been cited as the biggest drug threat to this region and the Northeast as of 2016 (117).

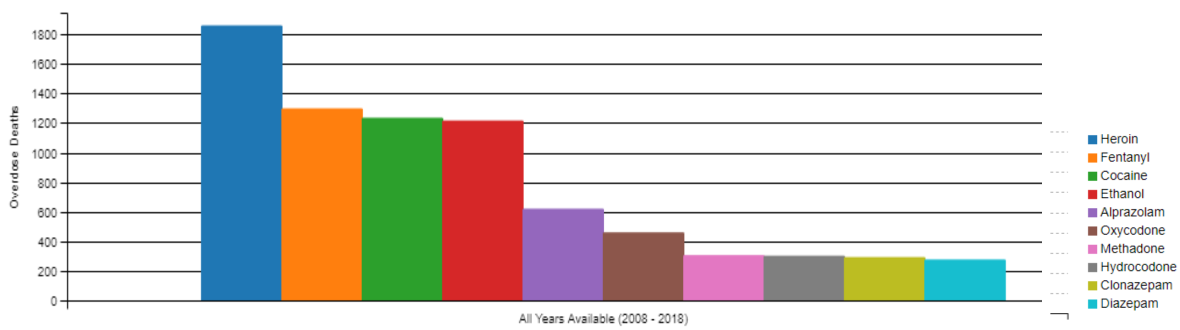

Figure 2: Number of Drugs present in overdose death, Allegheny County, PA, 2008- July 2018
*Data from Allegheny County Medical Examiner Office/ Overdose Free PA

Figure 2 highlights the 3,718 drug overdose deaths that occurred between 2008 and the midpoint of 2018 in Allegheny County, PA. The drugs that are contributing to the most deaths include heroin, fentanyl, cocaine and alcohol. The blue bar represents heroin (49.8%), the orange represents fentanyl (34.8%), the green represents cocaine (33.1%), and the red represents ethanol (32.6%). The remaining drugs include a variety of "prescription" opioids and benzodiazepines including oxycodone and alprazolam. Heroin has still contributed to the most deaths across this time frame (n=1853). In 2016, fentanyl contributed to 412 deaths and in 2017 it contributed to 547 deaths. In 2016, cocaine contributed to 221 deaths and in 2017 it contributed to 277 deaths. In 2018, there have been 86 deaths to date; fentanyl has contributed to more than 67% of these, and cocaine has contributed to 44.8%. Heroin has contributed to 39.1% (50)

3.0 DRUG EVIDENCE: A REVIEW OF RELEVANT LITERATURE

There are few peer-reviewed reports around illicit drug evidence in the public health literature; much of the information around illicit drug markets and drug evidence is found in criminal justice, demography, policy and sociology literature. The scope of those that exist range from analyses of drug policy, descriptions of urban markets, government surveillance reports. Few, analyses exist on the contents of drug evidence and rarely are they used for public health purposes based on our findings. Even fewer quantify drug evidence and categorize by drug contents.

3.1 METHODOLOGY

As of July 1, 2017, a preliminary literature search was conducted using typical public health search engines and PUBMED and OVID (Medline), with the following search terms: [stamp bag OR dope bag]. This failed to return any legitimate results, and thus the search terms were modified to include [stamp bag OR dope bag] AND [“heroin” OR “fentanyl” OR “opioids.”} This also failed to return any results. For comparison, a Google Scholar search was conducted using identical search terms but did not return additional peer-reviewed research. As a reference, the first ten pages listed news articles, online blog discussions, social media threads, congressional hearings, and books.

A second, broader search was conducted with the public health librarian using the same databases with different search terms [drug market OR heroin market] to capture more articles around illicit drugs and their sales. Our inclusion criteria included studies conducted in the United States or on populations in the United States to evaluate the ongoing national epidemic; we were interested in studies on local risk factors, local markets, or local law enforcement practices. We limited our results to English-language articles and excluded clinical trials, biographies, newspapers, and other designs that we were not interested in evaluating based on our search terms. One hundred and fifty-five articles were returned, and of these 121 (78%) articles were excluded based on title and abstract. Seventy-four (61.1%) were international studies, fifteen (12.4%) evaluated clinical elements of drug abuse, nine (7.4%) were not applicable to the search terms or were beyond the scope of illicit drug markets, seven (5.8%) reported on chemical makeup and toxicology of drugs, six (5.0%) evaluated behavioral aspects of drug use and initiation, four were mortality studies (3.3%), three (2.5%) evaluated HIV, two (<1%) evaluated opioid treatment, and one evaluated co-use of steroids and illicit drugs (< 1%).

The remaining 34 articles were reviewed for any mention or analysis of drug evidence, excluding articles that relied solely on questionnaires about cost of drugs as they ultimately were not relevant to the topic. Articles that include qualitative interviews to support data on heroin markets were evaluated for relevance. If the article mentioned stamp or dope bags, it was retained for immediate relevance to the topic.

Of these, 25 were excluded after article review due, language, non-relevant topics (injection drug use, personal monetary costs for drugs, agent-based modeling, prescription opioid diversion, illicit methadone sales, adulterants, mortality) or unavailability from restricted access or publishing dates prior to 1975. Upon completion of the article review, an additional three relevant articles were obtained through “snowball” searching references that were probable to contain information on stamp bags or dope bags. The table below details the articles that were found and deemed to be relevant to the topic of stamp bags and drug evidence in the United States. Articles that specifically mention stamp bags or quantify drug evidence are noted as compared to those that did not mention them or use them in any analyses As a note, using the search terms in 2018 will result in a single article that was published from his dissertation, so there has been little change over the course of a year with respect to the amount of literature on stamp bag surveillance.

Table 4: Literature review results for general search terms of [heroin market OR drug market] with the purpose of detecting peer-reviewed studies on stamp bags, conducted 2017

Citation	Classification	Study Type	Population and time frame	Primary Outcome	Main Findings	Relevant to stamp bags?
Mertz et al. J Forensic Sci. 2014 Nov;59(6):1583-5	Epidemiology	Descriptive; death certificate review	Sample of death certificates from overdose decedents in Allegheny County, PA	Proportion of certificates that were misclassified among those with morphine and heroin listed	Of 112 that listed morphine but not heroin, 74 were found to be heroin-related overdose deaths.	Mentions in text; not relevant
Lucyk & Nelson. Int J Drug Policy. 2017 Aug. (46):168-171	Epidemiology	Commentary	United States			No; illicit drug evidence mentioned
Gladden et al. MMWR 2016 Aug 26;65(33):837-43	Epidemiology	Descriptive; surveillance	United States, 2013-2014	Number of drug products containing fentanyl; fentanyl related overdose deaths	Fentanyl evidence submissions increased by 426%.	No.
O'Donnell et al. MMWR Morb Mortal Wkly Rep. 2017 Sep 1;66(34):897-903	Epidemiology	Descriptive; surveillance	United States, 2006-2015	Heroin, fentanyl and fentanyl-analog related deaths; fentanyl evidence submissions	Submissions from law enforcement increased for fentanyl products from 2006-2015.	No.
Mars et al. J Psychoactive Drugs. 2016 Sep-Oct;48(4):270-8.	Ethnography	Commentary; discussion using qualitative interviews	Philadelphia and San Francisco, current heroin injectors, 2012	Types of heroin sold; user opinions on quality	Powder heroin is more common on the East Coast vs. black tar in the West. Strength and duration of high were reportedly markers of high quality heroin.	Mentioned in the text as part of heroin market for Philadelphia

Table 4 Continued

Aldridge et al. Int J Drug Policy. 2016 Sep; 35:7-15	Market analysis	Cost analysis	1,031 vendors	Monthly sales revenue for online vendors.	Heroin and fentanyl did not contribute to most of sales.	No. Retained for use of dark web sales as a form of surveillance.
Mars et al. Soc Sci Med. 2015 Sep;140:44-53	Ethnography	Qualitative interviews	Philadelphia and San Francisco, current heroin injectors, 2012	Under-researched market influences on heroin use	Most interviewees were homeless or low income. Price, purity, dealer, and consumer knowledge are important for influencing a user.	Mentioned in text as part of Philadelphia's branding.
Unick et al. Addiction. 2014 Nov;109(11):1889-98	Epidemiology	Population-based study using DEA and hospital data	United States inpatient hospitalizations, 2008-2012	Number of heroin overdose hospitalizations	Heroin hospitalizations were associated with decreases in price but not purity (CI: 1-4.8)	No
Wendel & Curtis. J Drug Issues 2000. 30(2):225-260	Ethnography	Ethnographic study of heroin markets	300 users and dealers in New York City, 1996-2000	Stamp bag history, use, and current trends	In the late 1990s, stamp bags were disappearing in New York City as a regular vehicle for heroin.	Yes
Kotarba et al. Subst Use Misuse. 2010 Jul;45(9):1390-405	Ethnography	Qualitative study using observational and in-person interviews	Drug users in dealers from Houston Tx and New Orleans, LA, before and after Hurricane Katrina	Location, drug type, and other aspects of drug markets before and after the hurricane in New Orleans and Houston.	Only 26 respondents used heroin, though 15.3% of users in New Orleans tested positive for heroin compared to 6.5% in Houston.	No
Dunlap et al. J Psychoactive Drugs. 2009 Sep;41(3):219-26.	Ethnography	Qualitative study using observational and in-person interviews	Drug users in dealers from Houston Tx and New Orleans, LA, before and after Hurricane Katrina	Ease of obtaining illicit drugs upon evacuation, barriers to obtaining drugs	Interviewees found it easy to find illicit drugs upon relocating but were cautious to buy from just	No

Table 4 Continued

					anyone. Drug terminology differed between Houston and NO.	
Ciccarone, Unick & Kraus, Int J Drug Policy. 2009 Sep;20(5):392-401	Epidemiology	Trend analysis of heroin cost and purity	DEA data on price and purity across the U.S., 1993-2004	Mean price and purity of heroin by region of the U.S.	The price of heroin declined up to 80% in some US cities while purity remains the same.	No.
Ciccarone. Int J Drug Policy. 2009 May;20(3):277-82	Structured historical examination	History and detailed description of source of different types of heroin				No

3.2 KEY FINDINGS

3.2.1 Articles Under Review

Thirteen articles were under review, nine of which were obtained using the defined search terms. Four articles were obtained from searching references. Two sets of two articles use identical study populations to examine various aspects of the heroin market. Of these articles, only four mention “stamp bags” or “dope bags” in the article, and one article examines the history of the stamp bag (54). None of the articles utilize stamp bags as a form of illicit drug surveillance, though qualitatively they do examine the bags and how they might be used and tracked. However, there were articles that examined drug evidence as part of “surveillance” at the population level. (103,118) Additional articles on heroin trends in New York were not included as they did not add additional information beyond what was already included, nor did they address stamp bags directly.

3.2.2 Summary of Findings

Of the articles under review, the majority were ethnographic or epidemiologic studies that relied on qualitative interviews as their main source of data. There were four studies classified as population-based epidemiological studies that used surveillance data from medical, public health, and law enforcement databases. Two studies were also defined as epidemiological studies but ranged from record reviews to a review of literature and commentary. There were five ethnographic studies that used mixed methods to examine heroin markets, and two remaining studies that consisted of mix of a historical papers and revenue analysis for the dark web.

The epidemiological studies evaluated several outcomes as they relate to drug use and health outcomes. Two reported on opioid-related overdose deaths and the number of drug evidence submissions containing those drugs in the United States (103, 118). Unick et al (2013) evaluated hospitalizations for heroin as they related to heroin market characteristics. Ciccarone et al (2009) performed a trend analysis of DEA data to evaluate changes in price and purity across the United States. (68) In general, these studies reported consistent findings. Heroin-related deaths, hospitalizations, and drug evidence submissions have increased with an accompanying decline in price over time. Drug evidence submissions with fentanyl, and fentanyl overdose deaths, have also increased. While these studies incorporate drug evidence data to enhance their studies, none explicitly differentiate between different types of drug evidence or examine the ways in which illicit drug data could be used for this purpose.

The other two epidemiologic studies are different. The first mentions drug evidence and stamp bags in the manuscript, but the actual intent of the article is to evaluate the misclassification of morphine and heroin-related deaths from death certificates. (90). The second, broader article from Lucyk & Nelson (2017) examines and comments on the history of the opioid epidemic from a surveillance perspective and describes both the usefulness and the pitfalls of current toxicology methods as it relates to tracking overdose deaths. (11) While this is inherently tied to methods for illicit drug surveillance, their explanations were limited to human-sample screenings and urine analyses commonly found in hospital and toxicology labs.

The ethnographic studies are rich with detail with respect to heroin markets and factors that determine heroin use, but they are limited to similar and smaller populations in strict geographic areas of the country. Two studies describe interviews from the same population of injection drug users in Philadelphia and San Francisco, and two studies describe interviews from populations of users and dealers in Houston and New Orleans. The fifth ethnographic (54) but it is restricted to users in New York City.

The final group of articles are a mix of study types and classifications; none of the articles evaluate drug evidence (particularly stamp bags) as a form of surveillance. However, one study is a cost analysis of a “dark market” for illicit drugs, though the unit of analysis is the vendor and the subsequent revenue from illicit sales. One study is a broad historical examination of heroin markets but fails to examine the finer details of heroin branding and sales. (67)

3.2.3 Relevance, Strengths & Limitations

Though the body of research is not highly relevant to our methods and outcomes, it still represented a broad sample of study types, outcomes and populations. Four studies were population-based and are representative of the general population. Their findings can be generalized across the United States to anyone at risk of heroin-related overdose death.

In general, these articles were consistent in their themes and findings as they relate to heroin and the heroin epidemic, but they did not explicitly demonstrate how or why illicit drug data could be used to help inform surveillance, prevention, and planning in public health or law enforcement. Given the nature of the articles, the primary outcomes were not relevant to the study at hand and were rarely defined. This is what we expected to find given the limited number of articles from the initial searches.

Given the small sample sizes and unique geographic areas of the ethnographic studies, the findings are unlikely to be generalizable with respect to local markets, local drug vernacular, and user demographics. New Orleans and Houston are in regions of the United States where the heroin epidemic has less of a presence. (119) On the other hand, the findings of Wendel & Curtis, though unique to New York City, are highly relevant as context for the current dissertation. (54)

The ethnographic study samples resulted from snowball sampling, which is a non-random sample. However, snowball sampling is a purposeful way to sample; in this case, the population is typically inaccessible and therefore the best sampling technique was used for recruitment. (120).

3.2.4 Conclusions

Ultimately, few articles exist that examine the heroin and fentanyl epidemics using illicit drug evidence to describe the changes and patterns in drug availability in the United States. There is no public health, peer-reviewed articles that utilize drug evidence to enhance current knowledge of the epidemic at the detailed level of stamp bag trends, though there are some population-based studies that have incorporated drug evidence data into their surveillance. There is room for new research around this topic, and for examining the possibilities of using illicit drug data to enhance local, state and national surveillance.

4.0 PUBLIC HEALH SURVEILLANCE

Public health surveillance is "the continuous, systematic collection, analysis and interpretation of health-related data needed for the planning, implementation, and evaluation of public health practice." (121) Examples of well-known public health surveillance systems include mortality data, hospitalization data, and behavioral surveys. Beyond public health, there are many example surveillance systems such as crime surveillance, surveillance for substance abuse and mental health and field-specific mortality surveillance (122-124).

Syndromic surveillance has been defined as "an investigational approach where health department staff, assisted by automated data acquisition and generation of statistical alerts, monitor disease indicators in real-time or near real-time to detect outbreaks of disease earlier than would otherwise be possible with traditional public health methods." (125). An example of a "non-traditional method" for public health is the Drug Abuse Warning Network (DAWN), which is no longer in use. This system recorded emergency department visits where drugs were directly related to the admittance (126).

4.1 DISSERTATION SIGNIFICANCE

There are several key arguments for syndromic surveillance in public health literature. In most cases, syndromic surveillance systems have been utilized for the detection and investigation of infectious disease outbreaks or possible infectious terrorist threats (125, 127, 128). Syndromic is not meant to be a replacement for traditional surveillance, but rather a supplemental system for any number of possible events. (129) However, there has been some recent work around drug monitoring using these systems (130). Evidence from infectious disease studies suggests that these systems can use current data systems in place or supplement current practice and work well if they are automated or electronic. (127, 131) North Carolina's Disease Event Tracking and Epidemiologic Collection Tool (NCDETECT) is a good example of a syndromic event system that has been used to monitor heroin-related emergency department visits, among other poisoning-related events. (132). Because the system is near-real time, it has the potential to general more timely data compared to other data systems and can contribute useful data. (130, 132).

4.1.1 Supplemental Surveillance: Drug Evidence

This dissertation incorporates an aspect of surveillance; the argument is that the medical examiner stamp bag data offer timely information on illicit drugs that are circulating in the community. The data could possibly be used to supplement and enhance (but not replace) traditional illicit drug overdose surveillance sources. While the police records can lag a few days, the drug chemistry analyses are performed daily, and the results entered in near-real time. Much like any system, there is a lag in the time it takes to complete the analysis from the time the actual drug evidence was seized and submitted.

It aligns with the CDC definition of syndromic surveillance, particularly with regards to earlier detection of possible threats or changes compared to other traditional methods. Because this dataset and its procedures are already established, it can move closer to being real-time, limit the burden on stakeholders, and utilize fewer resources than if it was acute, “drop-in” surveillance for a sudden, unknown drug-related event. Acute surveillance usually occurs for a single event that will be short duration. (125) To our knowledge, this dataset has not been used in the form of syndromic surveillance.

4.1.2 Argument for Surveillance: Drug Evidence

Using the following body of evidence, we make the argument for expanding traditional public health surveillance for opioid-related outcomes, particularly with respect to illicit opioids, and considering new or different data systems to supplement current knowledge and shorten the time to data acquisition and analyses. For this dissertation, we built a database of illicit drug seizures where stamp bags are the primary unit of evidence and analyze drug patterns for those bags.

This dissertation has three aims. First, we aim to build an accessible surveillance database that is useful to multiple stakeholders such as law enforcement, drug chemists, toxicologists, and epidemiologists for illicit drug surveillance and research. We plan to analyze the demographic characteristics of individuals present at these seizures and describe the overall drug contents of these bags. We will acknowledge and detail the limitations of using these data, including specific sources of bias.

Second, we aim to analyze the spatial patterns associated with these stamp bags. For this analysis, we will use the drug contents and seizure cases as the unit of analysis. We aim to evaluate clustering patterns between 2010 through 2017 for heroin, cocaine, fentanyl, and fentanyl analogs.

Third, we aim to analyze and describe the rapid rise of illicit fentanyl in the county between 2010 through 2017 and publish a short surveillance report to demonstrate the rapidity of the data and the urgency of the issue. Finally, we will summarize our findings from our analyses and make specific recommendations regarding drug evidence data and future areas of research.

5.0 EXPANDING ILLICIT DRUG SURVEILLANCE: STAMP BAG DATA FROM A LOCAL COUNTY MEDICAL EXAMINER OFFICE

5.1 INTRODUCTION

Heroin and synthetic opioid-related deaths are increasing alongside deaths due to prescription opioids. (42) Between 2010 and 2015, heroin-related overdose deaths quadrupled, and other synthetic opioids and illicit drugs continue to fuel the increase in overdose mortality. (103, 133, 134)

Across the public health literature, the opioid epidemic has been quantified using health plan (135) hospitalization in-patient records (27-28), death certificates, prescription records (136-139) and surveys, which can be particularly helpful when capturing information on heroin and illicit drug use.(133, 140-142) Using these systems, investigators have been able to shed light into the epidemic. For example, possible mechanisms and contributing factors for heroin initiation have been identified. 8) Changes in drug patterns among overdose deaths have also been identified and monitored. (9)

5.1.1 Limitations of Current Systems

When it comes to specificity of drug-related overdose, public health surveillance systems do not always capture specific information on illicit drugs. Coding on death certificates for drugs can make detection of new or specific opioids difficult because they are often grouped into larger drug categories. (42) For example, from 1999 to 2015 nearly 35% of all drug poisoning death certificates did not specify the type of drug or drugs that contributed to the death for select states (143), though there have been vast improvements in detection and reporting using literal text. (7) With new illicit drugs appearing on the market, it is important that public health surveillance data are supplemented, or expanded, using alternative data sources to help shed light on the newest and potentially more lethal opioids.

5.1.2 Drug Evidence Data

Law enforcement data on drug evidence submissions can be extremely useful for public health officials. These data have demonstrated a significant increase in illicit fentanyl and fentanyl analogs out of local and state laboratories, from 924 submissions with fentanyl in 2013 to 3,344 submissions with fentanyl in 2014. (118) The United States Drug Enforcement Administration (DEA) also releases periodic nationwide alerts regarding new, unusual, or highly lethal drugs, such as U-47700. (144) Much of these data are pulled from the DEA's National Forensic Laboratory Information System (NFLIS), which collects drug chemistry data on illicitly manufactured drugs across the United States. (145) The DEA also reports detailed toxicology information for overdose decedents in collaboration with statewide coroners, medical examiners, and law enforcement. This level of detail is important and highlights the number of different opioids (and other drugs) that individuals are using. For example, in Blair County, Pennsylvania, specific benzodiazepines (alprazolam and clonazepam) were reported as the second and third top drugs found in overdose decedents. (146)

Though NFLIS and DEA reports are excellent for providing detailed, timely updates about drug activity, there are few peer-reviewed public health studies or public health reports that describe drug evidence in detail and none that consider its use for enhancing opioid surveillance. There are some examples of studies that detail heroin market trends, mention specific types of drug evidence or utilize NFLIS to report on evidence submissions. (90, 103, 118, 147, 148) This lack of reporting, in part, could be due to the variation in how heroin is sold and marketed across the United States. Sticky black tar heroin, for example, has circulated in the West and powdered forms in the East. (148) Another explanation is the variation and accessibility of data around specific types of drug evidence to public health researchers. One type of evidence that can be analyzed is stamp bags, otherwise referred to as a "dope bag." (54) Stamp bags are small wax packets that have an identifying marker, or stamp, and are used to package illegal heroin and other illicit drugs. In some cases, the bags will be unstamped. In Allegheny County, Pennsylvania, the medical examiner office collects and tests the contents of these bags to identify the different types of drugs being sold on the street and provide evidence for criminal cases.

5.1.3 Aim and Objectives

Drug evidence data, which contains information on drug contents and purity, is available in a timely fashion in Allegheny County. We aimed to develop an illicit drug surveillance system for use by public health, law enforcement, and the ME by merging data sources from law enforcement and drug chemistry for incidents of stamp bag seizures. To do this, we created definitions for categorizing and monitoring illicit drug in stamp bags, developed a sustainable data structure, developed quality control checks for matching, cleaning and measuring data, implemented rules for data cleaning, and described characteristics of the resulting database.

5.2 METHODOLOGY

5.2.1 Purpose and Data Source

Drug evidence is routinely submitted to the Allegheny County Office of the Medical Examiner (ACOME) by law enforcement for drug chemistry testing and is currently available for the years 2010 through part of 2018. The drug evidence is tested, and the results used for the purposes of criminal investigation. Data is entered into a database and identified by laboratory case number. Drug evidence results must also be submitted regularly to NFLIS.

5.2.2 Data Collection, Coverage and Sampling

The geographic coverage of this program extends to Allegheny County, PA but may include some cases from neighboring counties. Law enforcement drug seizures can occur as undercover drug purchases, planned or unplanned seizures, or from an overdose event. Law enforcement officials record information on the individuals present at the seizure and seize drug evidence to submit to the medical examiner office for testing. Law enforcement data include information on individuals present at a drug seizure; suspect name, sex, race, age, incident address and incident date. The report also includes the agency that submitted the evidence for testing (for example, City of Pittsburgh police, Zone 3). Due to limited resources, evidence that is linked to open criminal investigations must be submitted per the county submission protocol. This type of evidence is the priority for the drug chemistry unit and therefore they cannot routinely test evidence that does not have a criminal case linked to it. (149) a result, criminal evidence is overly represented among seized drug evidence that gets tested.

Drug evidence is tested daily in the drug chemistry unit of the Allegheny County Office of the Medical Examiner. Upon submission of a batch of evidence from a single case, scientists from the unit pre-sort the evidence into groups based on similar characteristics (including color, marking, packaging, and form). A single item from each group is then randomly selected and tested for controlled substances. Evidence is primarily tested using GC-Mass spectrometry along with additional tests (e.g. color reagent test). The drug evidence we analyzed were stamp bags. Below is a schematic that demonstrates how stamp bags are recovered from the community and ultimately tested in the drug chemistry laboratory.

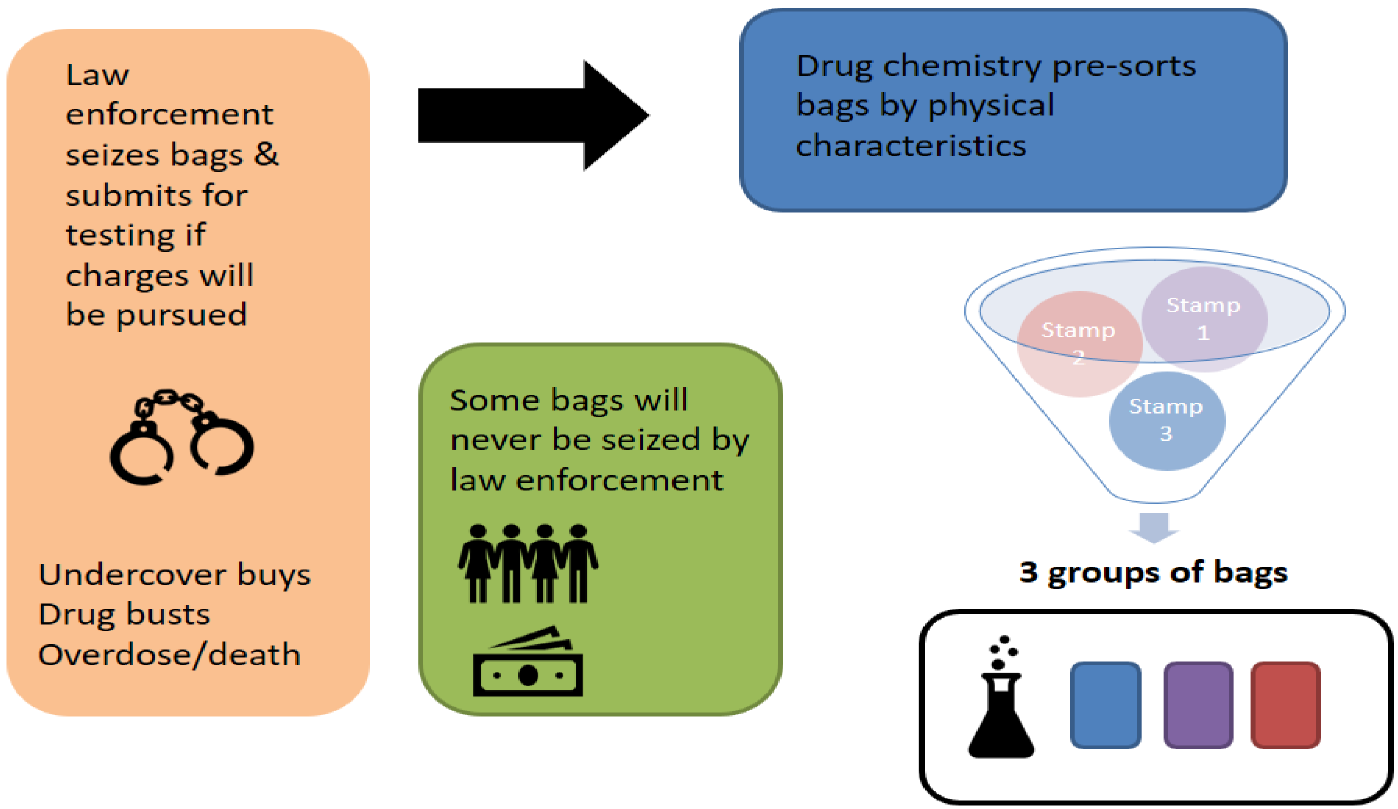

Figure 3: Schematic to show the processes behind data collection and sampling for stamp bags, Allegheny County, Pennsylvania

5.2.3 Medical Examiner Database

The final database that would be returned to the medical examiner office for future use was created by merging the drug chemistry data with the demographic data for all offense years. We retained only those records that had a corresponding stamp bag seizure. The final database listed each individual person that was present at the incident and matched all corresponding case data to each person.

5.2.4 Analytic Database Construction

The analytic database was created for the purposes of analyzing stamp bag contents, incident locations, and demographic data associated with stamp bag seizures. This database was de-identified and retained a single line for each tested bag, along with the matched incident location. Drug chemistry data for stamp bags linked with demographic data from law enforcement reports by unique case number and then further de-duplicated using laboratory item number. Cases with missing drug information were removed, as drug contents of the stamp bags were a primary outcome for our analysis. Incident locations outside of Allegheny County were excluded, as were cases where the offense date occurred prior to 2010.

To remove incident locations outside of the county, we printed a list of all submitting agencies and isolated those that were not associated with Allegheny County. The three major categories included agencies that submitted evidence from another county (such as Beaver County), federal agencies such as the FBI, DEA, and US Postal Service, and "other" non-specific agencies. From there, we reviewed each incident location for all these agencies to determine if the address fell within Allegheny County. If it did not, it was excluded from the database. Since the primary purpose of the database was to track illicit drug trends over time and geography, we only retained one address record per stamp bag regardless of how many people were present at the incident. In the final surveillance database that was used in this dissertation, population data was not retained since many individuals were present at each incident, and individuals were often present at multiple incidents. Final analysis variables are listed in the Results schematic.

5.2.4.1 Police Data: Demographics

Police data from 2010 through 2017 was obtained from the medical examiner office. A confidential statistical program was created to perform the de-duplication process using the Suspect Name identifier field, which would ultimately be removed for the analytic database. The datasets were combined and "Year" variables created to identify the year that the offense occurred. The following de-duplication steps were performed, in order, to remove duplicate individuals in the dataset across years and within years.

a. True duplicates were removed, as well as blank rows, by removing records with identical fields.
b. Duplicate individuals were removed where they had the same name, age, race, sex and offense date. This indicated that they had an offense on the same day.

   Ex: Mickey Mouse, male, age 100, mouse, 01/01/2018

   Ex: Micky Mouse, male, age 100, mouse, 01/01/2018
c. Duplicate individuals were removed where they had the same name, age, race and sex. This removed duplicate people with exact matching information.

   Ex. Minnie Mouse, female, age 99, mouse

   Ex. Minnie Mouse, female, age 99, mouse

d. For the purposes of demographic analysis and identification of unique people, we removed individuals with nicknames, confidential IDs, and initials. These people were retained in the merged database because we were uninterested in demographics and interested in stamp bag contents.

   Ex. D. the Duck, Goofy, Pluto. M.M., Mouse #101

Further, identifiers had to be removed for the purposes of analysis and no additional changes could be made to the database once they were removed.

Removing duplicates based on multiple fields always retained at least one record with some demographic information, starting from more fields (sex, race, age, offense date) to less fields (sex, race). When removing duplicates using just names, we found that we would often remove a record that had actual demographic information in it and retain one with missing information. Because of this, we could not exclude records on name alone:

Ex: Donald Duck, male, age 98, duck

Ex: Donald Duck, --, --, --

As a result, for the purposes of our demographic analyses we decided to remove records with missing information for all the following: sex, race and age. By doing this, we ultimately excluded the duplicated rows that did not contain information. We were able to check this in a series of steps that de-duplicated the data based on subsets where one variable was missing.

The final demographic dataset that was used for analysis included all unique individuals associated with stamp bag seizures that were seized and subsequently tested for controlled substances in the drug chemistry laboratory during 2010 through 2017 and had demographic information in the dataset. Descriptive statistics were calculated by year for age, sex and race.

The number of individuals with complete missing data is reported, but those individuals are dropped from the dataset.

5.2.4.2 Categorization of Stamp Bag Contents

The drug chemistry data were analyzed by drug type and seizure year, which is indicative of when the drugs were present in the community. The definitions in Table 5 were created after consulting the International Classification of Disease Codes – 10th Edition, the European Monitoring Centre for Drugs (150) and Drug Addiction and DEA reports. Though fentanyl and its analogs drive the synthetic opioid category, there were additional synthetic opioids found in stamp bags that were included in this category because they fit the synthetic category but were in small quantities. Because CDC uses the term "synthetic opioids" to in their *Morbidity and Mortality Weekly Reports*, we chose to categorize it this way. Though CDC often excludes methadone, we retained it. (103) We performed thorough searches of the stamp bag data to incorporate and correct for variations in spelling of drugs. Other drugs were also detected in stamp bags but were not reported for this paper due to small numbers. These drugs include amphetamines, acetaminophen, codeine, carisoprodol, gabapentin, and tryptamine. It is important to note that actual marijuana plant is not described here, but the THC which is a single cannabinoid and the primary psychoactive substance of marijuana.

Table 5: Drug Categorization for drugs found in stamp bags, select drugs, Allegheny County, Pennsylvania. 2010-2017

Category	Drugs (with or without others present)
Benzodiazepines	Alprazolam, clonazepam, diazepam, lorazepam, temazepam
Cocaine	Cocaine, cocaine base, cocaine HCl
Fentanyl	Fentanyl
Fentanyl Analogs	Acetyl fentanyl, butyryl fentanyl, furanyl fentanyl, carfentanil, cyclopropyl fentanyl, methoxyacetyl fentanyl, p-fluoroisobutyryl fentanyl, cis-3-methylfentanyl, trans-3-methylfentanyl, acryl fentanyl, benzyl fentanyl, valeryl fentanyl, phenyl fentanyl, U-47700
Heroin	Heroin, heroin HCl
Methamphetamine	Methamphetamine
New Psychoactive Drugs	AMB-Fubinca, ethylone, methylone, pentylone
Synthetic Opioids	Fentanyl, fentanyl analogs, meperidine, methadone, tramadol, U-47700
Semi-Synthetics	Oxycodone, oxymorphone, hydrocodone, hydromorphone, hydrocodone + acetaminophen, buprenorphine
THC	Cannabis, tetrahydrocannabinol, marijuana

*Data categorized using ICD-10, DEA, and European Drug Monitoring definitions and groupings.

The final drug chemistry dataset included all laboratory-tested stamp bags with associated police report information from stamp bag seizures, and where the offense date occurred between 2010 through 2017

5.2.5 Data Quality Checks

Data quality checkpoints were included as part of the overall database construction and analysis plan since it was complicated to construct and analyze. After each major step in the process, data checks were performed to ensure that each step worked, and that the quality of the data was retained. Each of these steps can be performed in SAS version 9.4.1 (151) or Microsoft Excel, which is an essential element of the process since SAS is not readily available at the local medical examiner office. Logic for each step was reviewed with personnel at the medical examiner office. All data checks included manual hand calculation checks and de-duplication, which could be replicated using any form of software.

5.2.5.1 Pre-Analysis Steps

1. When the drug evidence data were first exported from the case file system into Excel files, the STAMP field was checked for completeness. All stamp seizures were identified using the STAMP field.
2. The files were reviewed alongside the manager of the drug chemistry lab to confirm that the correct files were being used and that each record was a separate stamp bag test record. The matching logic was also reviewed.

5.2.5.2 Database Construction Steps

3. Once the data were imported into SAS and the demographic data merged with the drug chemistry data, the database required manipulation for the purposes of analysis. A final database that included identifiers would be left with the medical examiner office, but the analytic files were not allowed to contain individual names. This step requires statistical software but accompanying steps for how to test matching and replicate it in Excel were included in the notes that accompany the SAS code.

4. De-duplication was done in a series of steps and the total numbers reviewed each time. This can be done in Excel with a function.

5. The records were spot-checked to ensure that each case's records were present, and none had been excluded during the merge process.

5.2.5.3 Database Cleaning

7. For analysis, variables and records were removed as early in the process as possible with detailed notes as to why they were deleted, including records that fell outside of the study time frame and geographical area.

5.2.5.4 Database Analyses

8. Counts and proportions in SAS were manually checked in Excel. Figures and tables were set up in Excel with programmed calculations.
9. Mapping addresses were cleaned manually in a series of steps that will be described later, though this process was revised to move toward automation.

5.2.6 Sustainment and Replication

Sustaining, updating and replicating the methods of the database construction process was one of the key elements (and limiting factors) of the dissertation. For administrative and internal purposes, a database containing each individual person with each case and all its linked records were maintained and returned to the medical examiner. For illicit drug surveillance purposes, a de-duplicated and de-identified database was returned to the medical examiner with detailed instructions on how to add additional years of data, how to replicate processes performed in SAS in other software, and how to define drug categories to align numbers across years.

Additional data years can be appended to the original database; this can be done in any number of statistical packages or Excel. If the same construction and cleaning rules are applied, then the database should maintain continuity and estimates remain uniform in how they are calculated and presented over time. If internal data collection rules change or additional data fields are added to the raw data, then these can also be established as new data fields with the caveat that the data will be counted as “missing” for prior years.

Because SAS is not a program package that the medical examiner office currently keeps on its computers, the SAS procedures were translated into Excel steps where possible. During the construction of the database, Excel was used for some steps to ensure that it would work. Similarly, when geocoding addresses for incidents we used an open-access Geocoder that is freely available on a government website. This would ensure that other individuals could geocode using the same process regardless of their statistical program access.

For spatial analyses, the data were analyzed using software that was available to the medical examiner office from the county. However, open-access programs can be downloaded for free and used instead.

A comprehensive text document was created to record notes and procedural steps for the medical examiner staff as a key deliverable alongside the database and analyses. This document contains information like what is found in the dissertation methods but acts as an instructional document for individuals who may or may not have a background in analytics or epidemiology. This document is in the process of being completed.

5.3 RESULTS

5.3.1 Database Characteristics

The demographic and drug chemistry data are described separately below, followed by a description of the merged database. Exclusion criteria for the analytic database included offense dates outside of the study timeframe of 2010 through 2017, stamp bags that were not tested, incident locations outside of Allegheny County, and missing dates.

5.3.1.1 Police Data

As the figure below shows, there were 37,489 individuals in the initial dataset (including but not limited to offense dates in 2010 through 2017). After the first de-duplication step, there were 30 duplicates removed for a total of 37,459 individuals remaining. After the second de-duplication step, there were 552 individuals removed for a total of 36,907 individuals remaining. After the third de-duplication step, a total of 34,445 individuals remaining. This is the total that was merged with the drug chemistry database.

After the final removal of nicknames and confidential identifiers, there were a total of 34285 (91%) individuals remaining in the dataset out of the initial 37,489 individuals.

5.3.1.2 Drug Chemistry Data

There were 20,089 stamped bags in the initial dataset that were seized and tested by the drug chemistry unit at the Allegheny County Medical Examiner office up until Dec 31, 2017. After de-duplication of true duplicate records and those with the same laboratory case number and laboratory item number, there were 20,573 unique records of tested stamp bags. These included bags that were tested prior to 2010, as well as those with missing drug results or untested data.

5.3.1.3 Merged Demographic Data: Unique Records

Upon merging the demographic and drug chemistry data for demographic analysis, there were 19981 records that matched to a corresponding laboratory case number with a stamped bag. We removed 6163 records that were duplicated in the merge because they were linked to multiple laboratory entries for 13818 records. We then removed non-county cases and cases prior to 2010, as well as exact matching names, for a total of **12019 unique person records** for 9634 cases, regardless if they had blank fields for age, sex, and race.

5.3.1.4 Merged Demographic Data: Unique Cases for Analysis

Without removing matching names but removing non-county cases and records prior to 2010, we retained 13518 records. Of these data, 3802 (28.1%) were missing information on sex, 4255 (31.5%) were missing information on race, and 4928 (36.4%) were missing information on age. After removing records with no demographic information (n=3768) for the purposes of deleting out final duplicated records, we retained **9750 unique records for 7762 cases** for demographic analysis. This was our best and most accurate estimate of unique individuals that had demographic data to analyze.

5.3.1.5 Merged Analytic Data

Upon merging the demographic and drug chemistry data, we retained 21945 records. After removing duplicated entries from the merge, we retained 20573 records (which is the total stamp bags in the raw data). After removing records with offense dates prior to 2010 and missing date information, we retained 18337 records. After removing 65 records where the incident occurred outside of Allegheny County, we retained 18272 records. After removing records where the stamp bag results listed “not analyzed” or were blank, we retained 16954 stamp bags associated with 10619 unique lab cases *that had demographic information* between 2010 through 2017.

This number is less than the total number seized and tested in the raw datasets due to linkage with demographic data (some cases are not entered into system yet), de-duplication of true duplicates, removal of all duplicates in the initial police file, and removal of cases that did not fit the study criteria. The figure below shows a step by step process to create the final analytic database. For the analytic database, the field for suspect name was dropped.

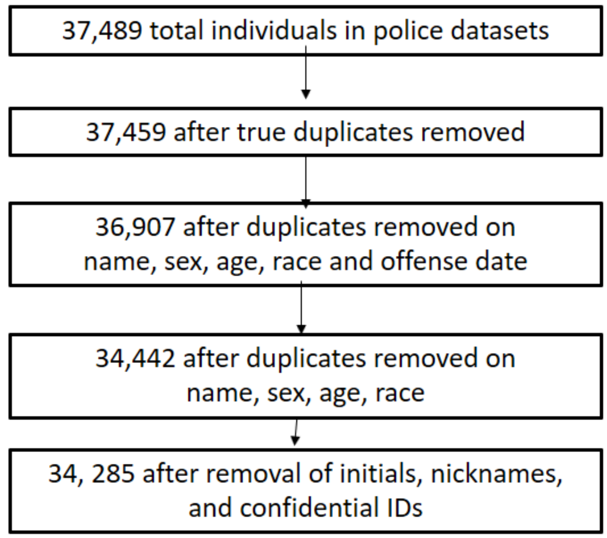

Figure 4: Stepwise de-duplication of the demographic police dataset, Allegheny County Medical Examiner Office

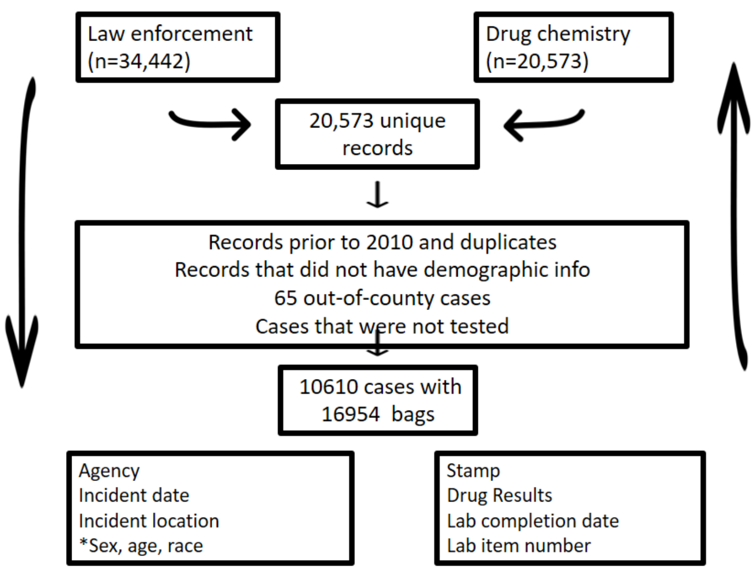

Figure 5: Final stamp bag database and resulting analytic variables, Allegheny County Medical Examiner Office, PA

*Note that additional de-duplication steps are not shown but removed additional records that were duplicated because of the merge.

5.3.2 Demographic Results

From 2010 through 2017, there were 12019 distinct individuals associated with stamp bag seizures where the bags were seized, selected and tested for controlled substances. Of the total 13518 individuals that we started with, 3768 (27.9%) had no information for sex, race or age and therefore were not included in the analysis. The remaining 9750 (72.1%) unique individuals had demographic information that could be analyzed.

Of these 9750 individuals, 7426 (76.2%) were male, 2284 (23.4%) were female, 6 (<1%) were undetermined sex, and 34 (0.3%) had missing information on sex. For race, 5504 (56.4%) were white, 3659 (37.5%) were black, 44 (0.4%) were of an unidentified race, 22 (0.2%) were another race, 25 (0.3%) were listed to be Hispanic (not a race), 9 (0.1%) were Asian or Indian, and 487 (5.0%) were missing information for race. For age, 1160 (11.9%) were missing information. The total numbers in 2017 drop off compared to 2016, which could ultimately be a function of the lag in testing and data entry.

The population of unique individuals associated with stamp bag seizures was primarily male (7426; 76.2%) and white (5504; 56.4%). Over time, this did not change; in 2010, there were 225 males (78.4%), in 2011, 178 males (78.4%), in 2012, 257 males (78.8%), in 2013, 1074 males (77.9%), in 2014, 1631 males (75.7%), in 2015, 1694 males (76.7%), in 2016, 1492 males (76.3%), and in 2017 875 males (74.1%). By year, the proportion of the population that was white was more variable but remained steady; 2010 (148; 56.5%), 2011 (124; 57.7%); 2012 (176; 57.1%), 2013 (809; 62.0%), 2014 (1231;61.0%) 2015 (1294; 60.7%), 2016 (1132; 59.9%), and 2017 (590; 52.3%).

Table 6: Demographic characteristics of unique individuals associated with stamp bag seizures and with demographic data available for analysis, by year of seizure. Allegheny County, Pennsylvania, United States, 2010-2017 (n=9750)

Sex	**Total (n=9716)**	**2010 (n=287)**	**2011 (n=227)**	**2012 (n=326)**	**2013 (n=1378)**	**2014 (n=2154)**	**2015 (n=2209)**	**2016 (n=1955)**	**2017 (n=1180)**
Male	7426 (76.4)	225 (78.4)	178 (78.7)	257 (78.8)	1074 (77.9)	1631 (75.7)	1694 (76.7)	1492 (74.5)	875 (74.1)
Female	2284 (23.5)	62 (21.6)	49 (21.6)	69 (21.2)	304 (22.1)	522 (24.2)	514 (23.4)	459 (23.5)	305 (25.8)
Race	**Total (n=9263)**	**2010 (n=262)**	**2011 (n=215)**	**2012 (n=308)**	**2013 (n=1304)**	**2014 (n=2025)**	**2015 (n=2131)**	**2016 (n=1890)**	**2017 (n=1128)**
White	5504 (59.4)	148 (56.5)	124 (57.7)	176 (57.1)	809 (62.0)	1231 (62.1)	1294 (61.0)	1132 (59.9)	590 (52.3)
Black	3659 (40.4)	110 (42.0)	86 (40.0)	127 (41.2)	481 (36.9)	774 (38.2)	821 (38.5)	737 (39.0)	523 (46.4)
Age	**Total (n=8590)**	**2010 (n=258)**	**2011 (n=214)**	**2012 (n=314)**	**2013 (n=1230)**	**2014 (n=1913)**	**2015 (n=1898)**	**2016 (n=1707)**	**2017 (n=1056)**
	28 (23-35)	28 (24-34)	26 (21-34)	27 (22-32)	27 (22-33)	28 (23-35)	28 (23-35)	29 (24-36)	28 (23-36)

*Data from the Allegheny County Medical Examiner Office.
[1]Missing data not shown. Separate N shown for each category.

5.3.3 Stamp Bag Contents

Of the 16954 seized and tested stamp bags between 2010 through 2017 that were linked to police data, 15756 (92.9%) contained heroin, 14666 (86.5%) contained heroin alone, 1779 (10.5%) contained synthetic opioids, 1548 (9.1%) contained fentanyl, 626 (3.7%) contained fentanyl alone, 133 (0.8%) contained cocaine, 7 (0.0%) contained cocaine alone, and 343 (2.0%) contained other synthetic opioids or fentanyl analogs. Fentanyl drove the increase in synthetic opioids alongside the increase in fentanyl analogs. The table below shows the proportion of bags that contained each drug over time.

Over time, the drug contents of the sampled and tested stamp bags changed. In 2010, 1663 (97.1%) contained any heroin, while zero bags contained fentanyl. In 2014, 59 (2.0%) of tested bags contained fentanyl, 237 (7.8%) in 2015, 641 (23.1%) in 2016, and 610 (43.3%) in 2017. Similarly, other synthetic opioids and fentanyl analogs appeared in tested stamp bags in 2015 (57; 1.9%), but in 2017 were present in almost 16.8% of stamp bags (n=237). The proportion of tested bags with cocaine also varied over time, from 11 (0.6%) in 2010 to 29 (2.0%) in 2017. Other drugs, such as the semi-synthetic opioids, marijuana and benzodiazepines, stayed relatively stable over time.

Table 7: Number and percentage of laboratory-tested stamp bags that had police information containing any major controlled substance, by category and year of seizure. Allegheny County, Pennsylvania. United States: 2010-2017

	Total (n=16954)	2010 (n=1712)	2011 (n=1314)	2012 (n=1503)	2013 (n=2321)	2014 (n=2885)	2015 (n=3037)	2016 (n=2777)	2017 (n=1405)
Drug Category (N, %)									
Heroin	15756 (92.9)	1663 (97.1)	1283 (97.6)	1469 (97.7)	2277 (98.1)	2813 (97.5)	2912 (95.9)	2440 (87.8)	899 (64.0)
Heroin alone	14666 (86.5)	1652 (96.4)	1276 (97.1)	1459 (97.1)	2267 (97.7)	2742 (95.0)	2688 (88.5)	1999 (72.0)	583 (41.5)
Synthetic Opioids	1779 (10.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	61 (2.1)	258 (8.8)	681 (38.3)	768 (54.7)
Fentanyl	1548 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	59 (2.0)	237 (7.8)	641 (23.1)	610 (43.4)
Fentanyl alone	626 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	9 (0.3)	63 (2.1)	245 (8.8)	309 (21.9)
Fentanyl Analogs	343 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	57 (1.9)	49 (1.8)	237 (16.8)
Cocaine	133 (0.8)	11 (0.6)	7 (0.5)	7 (0.4)	8 (0.3)	9 (0.3)	19 (0.6)	42 (1.5)	29 (2.0)
Cocaine alone	7 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	1 (0.0)	4 (0.1)	1 (0.0)
Benzodiazepines	6 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	0 (0.0)	2 (0.1)	2 (0.1)	0 (0.0)	1 (0.1)
THC	8 (0.1)	0 (0.0)	4 (0.3)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.1)	0 (0.0)
Semi-Synthetic Opioids (no codeine)	13(0.1)	1 (0.1)	1 (0.1)	0 (0.0)	0 (0.0)	9 (0.3)	2 (0.1)	0 (0.0)	0 (0.0)
Methamphetamine	9 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2(0.0)	7 (0.5)
New psychoactive substances[1]	73 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	2(0.0)	9 (0.3)	34 (1.1)	20 (0.7)	8 (0.1)

*Data from the Allegheny County Medical Examiner office.
[1]New psychoactive substances includes alpha-PVP, AMB-FUBINICA, 4-chloroethcathione, dibutylone, ethylone, n-ethylpentylone, methylone, mexedrone, and pentylone.
[2]Drug categories are referenced in the text, but results show total number and percentage of bags with any detection of the substance, with or without other drugs present. Categories not mutually exclusive. Other drugs not shown

5.4 DISCUSSION

In Allegheny County, Pennsylvania, 16954 stamp bags were seized; these bags could be linked to police data to identify the date they were seized on. These bags were used to develop an analytical, surveillance database to describe trends among the population and drug contents associated with these bags. In addition, the database was used to identify very specific synthetic opioids of interest, including fentanyl analogs, that may otherwise not be identified from death certificates.

Illicit synthetic opioids are not limited to heroin and fentanyl in the United States, and it is important to detect new and potentially more lethal synthetic opioids that are made available to users on the street. It is challenging to capture information on illicit drugs, which do not have a dedicated public health surveillance system to collect data and monitor changes. One source of illicit drug data is drug use surveys, which can provide good estimates but has typical methodological constraints such as self-reporting bias. While there have been reports of drug chemistry cases (115) in toxicology literature, toxicology results are more commonly reported from overdose fatalities. (99, 152) It is equally challenging to capture new or less frequent synthetic opioids (excluding fentanyl) or fentanyl analogs using only traditional methods of public health surveillance, such as death certificates, since synthetic opioids are often grouped into a single coded category. (41)

5.4.1 Main Findings

Of the 16,954 seized and tested stamp bags that could be linked to police data between 2010 through 2017, 15756 (92.9%) contained heroin, and 86.5% contained heroin as the only controlled substance in the bag. The proportion of bags that contain fentanyl has increased from 1 (0.0%) bag in 2013 to 610 bags (43.4%) in 2017; prior to 2013, fentanyl was undetected in stamp bags. While fentanyl analogs have gained a lot of media attention and have been more prevalent in different states (103), they were present in less than one percent of stamp bags.

There were 12019 unique individuals identified in the entire database. Only 9750 cases were found to be unique and have data for demographic fields, posing a challenge for analysis. Of those individuals, the majority were white (59.4%) and male (76.4%). The median age of unique individuals was 28 years old.

Our findings are consistent with reports from NFLIS and alerts from the DEA on the most dangerous illicit opioids on the market, especially in Pennsylvania (116, 153) yet highlight some other unusual synthetics as well. These findings support the notion that collaborative efforts on surveillance are key to examining and explaining gaps in evidence around drug supply and markets, and their downstream consequences on health. (67-68) This was also the one of the first instances of cyclopropyl fentanyl that was detected in drug evidence in the United States upon comparison to the NFLIS database. (145) These findings must be interpreted with caution, however, since they are limited by how much drug evidence can be tested as a function of resources. In 2017, we see that the number of bags declines in general in our sample, which can be attributed to a lag in testing and data entry. If we were to re-analyze the data in six months, the total numbers in 2017 would likely increase (but the proportions remain the same).

Neighboring states can use these results in context of what their own drug evidence shows, and might find the methods useful for monitoring drug evidence and quantifying illicit drugs. Reports and press releases from regional DEA offices, for example, suggest that other states across the Northeast see heroin as a leading drug threat. (154-155) Additionally, we know that other counties in Southwestern and Central Pennsylvania have detected fentanyl in their stamp bags from drug chemistry data that the county analyzed (data not shown). The methods from this analysis can also be adapted internally and externally to other types of drug evidence. Unfortunately, the evidence is not always categorized in a way that it can be separated out for analysis.

5.4.2 Limitations

There are several limitations to this study. First, the study sample represents a portion of all evidence that is collected by the laboratory and selected for testing. These items are overly representative of criminal activity, as these are the items that get priority attention. Second, given limitations of instrument capacity, staff and time, only a single bag is tested from each group of similar stamp bags. While we can reasonably assume that the bag selected from this group is representative of the remaining bags, we cannot truly estimate the total number of bags with each drug in the population.

For simplicity, we do not describe co-occurring drug patterns, such as mixtures of cocaine and fentanyl, which have been shown to be important with respect to overdose. (156) We also do not examine trends among the stamps themselves. Though it is difficult to examine the stamps due to sheer number, new data collection protocols and data elements are being developed and improved for future surveillance and monitoring by the unit. Finally, this is a cross-sectional, descriptive report using data from 2010 through 2017. Though we can ascertain the time at which these drugs were detected in drug evidence, we cannot make any inferences about risk of overdose, nor can we infer any causal associations with overdose or mortality.

Demographic data became more complete over time due to changes in reporting and data collection systems. Still, many individuals in this dataset were repeatedly found at each incident across time. This isn't unexpected, since we know that individuals who buy or sell drugs can repeatedly buy and sell (157-158). These estimates cannot be stratified by transaction type, however; the data do not differentiate between users or dealers. Given the sensitive nature of many of these cases, we would not have been able to publish such detailed information to preserve the confidentiality of the cases and protect law enforcement. With that context, we do not assume that our demographic results are representative of all individuals who use drugs since we have a mixed population. Finally, the construction of the databases used for these analyses was time-consuming and required a lot of cleaning. Though the process could be automated, it required several checks and re-constructions to ensure that the matching process was working. Removing duplicate values was especially challenging and had to be done differently for different parts of the project.

The findings in this study demonstrate the availability and timeliness of drug chemistry data in Allegheny County, Pennsylvania and highlights the ability to detect new synthetic opioids. Illicit drugs, including synthetic opioids and designer drugs, are quantified over time. Data on illicit drugs can be used to supplement and enrich current public health surveillance and continue to help explain the growing trend of opioid mortality attributable to illicit synthetic opioid overdose. Most importantly, it can be used to educate stakeholders and responders on prevention and harm reduction with respect to rapidly changing drug patterns in a community.

As these data systems are updated and improved, there will be several additional areas of applied research for evaluation of drug evidence

5.4.3 Addition to the Literature

The findings in this study demonstrate the availability and timeliness of drug chemistry data in Allegheny County, Pennsylvania and highlights the ability to detect new synthetic opioids. Illicit drugs, including synthetic opioids and designer drugs, are quantified over time. Data on illicit drugs can be used to supplement and enrich current public health surveillance and continue to help explain the growing trend of opioid mortality attributable to illicit synthetic opioid overdose. Most importantly, it can be used to educate stakeholders and responders on prevention and harm reduction with respect to rapidly changing drug patterns in a community. As these data systems are updated and improved, there will be several additional areas of applied research for evaluation of drug evidence.

6.0 SPATIAL PATTERNS OF ILLICIT OPIOIDS AND COCAINE: STAMP BAG ANALYSIS

6.1.1 Person, Place and Time: The Opioid Epidemic

The opioid epidemic continues to result in devastating mortality in the United States. From 1999 to 2015, middle age whites experienced an increase of more than 700,000 years of potential life lost (YPLL) because of the opioid epidemic. (159) In 2016, the opioid epidemic was responsible for more than one million years of potential life lost (160) which was particularly high among young adults (12.9 per 1,000 population ages 25-34 years old). Emerging epidemiological patterns have become evident across person, place and time for the epidemic in the United States. As of 2016, forty percent of overdose deaths involved a prescription opioid. (161) There is clear evidence that individuals with a higher risk of opioid-related overdose are white, middle-aged males (28, 33, 34) though the gap among all demographic groups is narrowing. (162)

6.1.1.1 Regional Patterns

Geographically, there are distinct patterns for opioid-related overdose death. The rates of prescription opioid overdose death were higher in areas of the Appalachian and southern United States (20, 35) while regions in the Northeast and Midwest had high rates of death due to heroin and fentanyl. (119) Geographic patterns of substance abuse, opioid abuse and drug overdose have been established and consistently reported using both survey data and GIS methods (36, 75, 163-166) at all regional levels. Most of these studies use survey or public health surveillance data to evaluate geographic patterns for various elements of the opioid epidemic.

6.1.1.2 Time Trends

Over time, the pattern of opioid use and overdose has undergone a stark changed. In 2018, the Food and Drug Administration produced a comprehensive report detailing the changes in the quantities of prescription opioid analgesics over time, including the total quantity sold to retailers, the total sold to customers, and the total quantities sold by price. While there was no apparent relationship between how much was purchased and the overall price of each drug, there were sharp increases in the early 2000s for total quantity sold. In 2010, the average morphine-milligram equivalent of opioids sold was 250 billion with a slow decline after that. (167) Even more recently, a study of Medicare and Medicaid recipients showed that prescription opioid use had not declined in this population from 2007 through 2016. (168) Still, in the past decade prescription opioids were more likely to contribute to drug overdose deaths (42, 106), while recently illicit opioids have contributed more heavily than legally prescribed semi-synthetics. (42, 47, 106)

6.1.2 Elements of Person, Place and Time: Heroin

The epidemiological trends for person, place and time are less specific among individuals who misuse, abuse and overdose from heroin. For example, rates of heroin overdose have dramatically increased across all demographic groups (72, 87, 162) There are mixed findings on whether heroin mortality and use has been clustering in urban or rural areas; as a historical rule of thumb, heroin was restricted to the inner city. (54, 77) There are far fewer geospatial analyses that focus entirely on illegal drugs, particularly those drugs that are sold on the streets. Much of the mapping that describes the heroin epidemic has been generated via news report with data from the CDC or the CDC itself. There are no public health reports that examine geographic heroin patterns down to street-level clustering of illegal drugs, which ultimately requires data from law enforcement. In Allegheny County, we have obtained a dataset from law enforcement and the medical examiner that contains drug toxicology evidence from drug seizures across the county with geographic information.

6.1.2.1 Stamp Bags and the Adulterated Heroin Market

Stamp bags, which are small wax packets used to package and sell heroin in some parts of the country, are collected as drug evidence by local law enforcement. This occurs primarily in the Northeastern United States (54, 91, 154) where heroin is typically sold in powder form (52). There is evidence that many users do not know exactly what sort of drug mixture that they are getting when they purchase it, which can make stamp bags dangerous. (162) When drugs are recovered by law enforcement, there can be multiple bags present at any one incident. The image (Figure 16) in Chapter 7.0 is an example of a stamp bag from Allegheny County.

6.1.3 Applicable Methodology

Mapping is a common methodology for visualizing spatial facets of the epidemic. In a surveillance report from New Hampshire, for example, mapping has been used to visualize drug trafficking routes and the locations of treatment providers across the state. (169) In peer-reviewed literature, several analyses have found clustering effects for opioid mortality or opioid-related injuries in the United States (164, 170) Perhaps unsurprisingly, investigators found that drugs do indeed cluster. As a point of interest, the hot-spot analysis showed that rural areas can be both "hot" or "cold", depending upon their location in the United States. (164, 171) There also have been other methodologies for spatial associations among opioid-related outcomes such as Bayesian spatial models at the zip code level (172-173), simple thematic mapping or overlays of data (75) proximity analyses at the census tract level (174) and longitudinal analyses of drug activity among neighborhoods (175). Investigators found that drug activity clustered in specific neighborhoods, but ultimately improved in areas where major reconstruction and development projects were in place. (175), suggesting that there are economic and social influences on drug markets and their ultimate health outcomes.

6.1.4 Objectives

In this series of analyses, the objective is to describe spatial patterns among stamp bags and their spatial patterns in Allegheny County over time. Our approach is unique in that we used incident address data for illicit opioids and mapped point locations of these incidents rather than rates, and we chose to evaluate spatial patterns using best practice per the Department of Justice manual for *Understanding Hot Spots*. (176) Unlike Rossen et al (2014) and Marshall et al, we analyzed local level drug data (and not mortality data) down to the block group level of sensitivity for a more granular and detailed picture of the epidemic. (164) We chose to use unique cases (that could have one stamp bag or multiple bags) as our unit of analysis to adjust for multiple observations at each location. We hypothesized that there will be spatial clustering of stamp bag cases, but these patterns will be random over time. We hypothesize that the clustering will be evident at the level of the case, and that most of the clustering will occur near urban centers.

To our knowledge, there are no similar studies in the public health literature that investigate geographic patterning of illicit drugs at the local level using stamp bag data from the police and medical examiner. This includes heroin, illicit prescription drugs, cocaine, methamphetamines, and other illegal drugs. Online surveillance tools can be used to demonstrate simple clustering by plotting the number or rate of overdose-related deaths (50) and the designated high-intensity drug-trafficking areas (HIDTA) from the DEA. We DO expect to find consistency with reports and online tools that have measured clustering of opioid mortality (164), opioid prescribing (178) and general drug activity (175), especially those that find clustering of illicit opioid mortality in urban areas. (171) Though we have not found actual studies that assess stamp bag clustering at the local level, we assumed that the stamp bag seizure incidents would also cluster in urban areas within Pittsburgh.

6.2 METHODOLOGY

The following analyses were performed using the master surveillance database, containing data on all stamp bag seizures from 2010 through 2017 where there were drug chemistry results, seizure dates, and addresses within Allegheny County. Each address is mapped within Allegheny County and then visualized using the drugs within stamp bags. The primary drugs under consideration for these analyses are heroin, cocaine, fentanyl, and fentanyl analogs. The Department of Justice *Mapping Crime* (176) manual was referenced to determine the most appropriate methods for visualizing drug activity over small regions with the purpose of detecting very high intense areas. As a result, we chose to map bags in our thematic maps and cases in the hot spot analyses.

6.2.1 Constructing and Cleaning Data Files

The database was created and the methods for this are described in Chapter 5.0 of this dissertation. The addresses of the incidents were cleaned so that the probability of mismatching during the geocoding process would be reduced. Because there is no way to obtain further information about each address other than the address field, we developed a pre-cleaning step that narrowed down the location of each address using the agency that submitted the incident. This helped to reduce error in pin-pointing addresses that were common ("123 Main Street") across many municipalities and helped to identify the correct coordinates when no municipality, state or zip code was listed. The following steps were taken to clean addresses:

1. Incidents were sorted by seizure year and submitting agency. Each agency's observations were reviewed in order by year to ensure consistency of street names and zip codes.
2. New address fields were added to the database for street name and house number, municipality, state, and zip code.
3. Address entries with incomplete information (such as street name, municipality, or zip code) were searched in an online search engine and entered the new separate fields. The

submitting agencies were used to help determine the correct municipality, especially for townships and boroughs. Full entries were parsed out into the corresponding fields.

4. Entries that only listed the municipality and state (such as Pittsburgh, PA) were parsed and geocoded to the centroid of the municipality where possible. As a note, we ultimately mapped with and without these because they detracted from our street-level detail.
5. Entries that listed a street within a municipality (such as Main Street) were parsed, but ultimately dropped for inability to pinpoint accurate coordinates.

6.2.2 Geocoding

We geocoded addresses using the open-access, web-based US Census Geocoder to the 2010 US Census records to have the most complete census year of data. (178) Correspondingly, we used the 2010 TIGERLINE Shapefiles from the US Census. (179) Once the geocoding process was complete, we reviewed non-exact, tied and non-matched entries. In the event an address is "tied", there are at least two candidate addresses that the original can be matched to. For the tied addresses we re-matched them using the single line option in the US Census Geocoder. (178) If records were non-matched, we attempted to improve or further clean the address field if possible. Entries with missing address information, and entries where the address could not be geocoded, were ultimately dropped from the analysis. After geocoding the dataset, we projected the data using North American Datum (NAD) 1983. (180)

6.2.3 Descriptive Statistics

We calculated descriptive statistics using ArcGIS (181) and Microsoft Excel during geocoding. We calculated the proportion of matched, tied, and non-matched records, as well as the proportion that were re-matched. We calculated counts of unique cases, as well as counts of stamp bags, and mapped them using thematic, aggregated mapping to evaluate overall burden of heroin activity.

6.2.3.1 Unit of Measure

The unit of measure for the analyses was an incident, or “point” on a map. We did not calculate and map rates because we could not reliably estimate the true numerator and denominator for each region. Given the lack of resident addresses for each person in the database, we could not assess whether the individuals at the incident scene (counted as part of the numerator) resided in that geographic area (part of the denominator). Since our primary outcome was not a statistical comparison between regions, we decided to use point data in our analysis and limit our conclusions based on that. Given that limitation, we approach our analysis two ways. First, we created thematic maps based on aggregated data points to visualize areas with high volume of stamp bags. Second, we utilized hot spot analysis to identify areas of high and low clustering.

Ultimately, this approach was favored over broad autocorrelation measures. Eck et al noted that these methods work well for point data and that starting with more simplistic, concentrated mapping can help to identify very low-level “hot spots”, and it was concluded to be a good first step in determining true high-intensity areas of activity. (176)

6.2.4 Mapping: Thematic Aggregate Maps

The first method employed was to aggregate counts of the total number distinct seizure incidents and total number of bags with each drug by zip code, census tract, and block group. Counts were totaled within each distinct polygon (region) and visualized using gradient thematic maps in ArcMap 10.6. (181) This gave us a visualization and estimate of regions that had the largest amount of activity across the county, as well as the largest number of bags that tested positive for each drug. As a caveat, multiple bags can be recovered from a single case, so we chose to also map distinct cases to account for that. The general procedure for this is as follows:

1. Within ArcMap, navigate to the Catalog and create folder links to wherever your data is stored. A simple choice is to store data in a .xls file and keep shape files in separate folders on the Desktop.
2. After navigating to your data, add the zip code shapefile for Allegheny County to the map, as well as the shapefile for three rivers. Add the City of Pittsburgh boundary file as well. This can be done by selection features or by adding a pre-created shapefile.
3. In order to map across years and drugs, first visualize the X and Y coordinates on the map, and then use "Properties" to query and select specific years or drugs.
4. After applying limits, join the zip code shapefile to the newly limited point shape file (for example, heroin bags in 2010). Select "Sum" as well as count for your outputs.
5. When the joined layer appears, go into "Properties\Symbology" and choose a method to visualize the data. Use gradient color schemes with natural jenk cut points.

6. After adding a legend and exporting the map, return to Data View and repeat for all drugs, all years, and all levels of geography.
7. The legend values were adjusted to Equal Intervals, with manual adjustment to ensure that maps could mostly be comparable across years.

6.2.5 Mapping: Localized Hot Spot Analysis with Getis-Ord i

The second method employed was to map each unique case (by drug type) at each of the three levels of sensitivity. We performed a local measure of autocorrelation known as hot-spot analysis to identify significant areas of concentrated illegal drugs versus areas with very little clustering. Hot spot analysis identifies significant clustering as measured by the deviation above or below a mean value. A specific feature and its neighbors must have similarly high or low values of *i*. For the purposes of this analysis, we plotted each observation as a point on the map rather than as a rate or ratio. The findings from this analysis, therefore, are more appropriately used for resource allocation and planning rather than for making conclusions about how different areas compare to one another. For our spatial relationship and weights, we selected the default distance estimate, rather than the nearest neighbor index (170), to introduce less bias.

The global outcome measure for hot spot analysis is Getis-Ord*, which is a z-statistic: n is the total number of features, $w_{i,j}$ is the spatial weight, and x_i is the value for j. See ERSI online (2017) for a complete description of the formula at the following location: http://pro.arcgis.com/en/pro-app/tool-reference/spatial-statistics/h-how-hot-spot-analysis-getis-ord-gi-spatial-stati.htm

6.3 RESULTS

6.3.1 Descriptive Statistics

In an initial mapping file, there were 18,136 available records in our surveillance database that were captured within Allegheny County, Pennsylvania between 2010 through 2017 that we tried to geocode. After an initial data cleaning, 7,285 (40.2%) addresses did not match, 459 (2.5%) were tied, and 10,392 (57.3%) were matched. Of the matched records, 2,600 (25.0%) were non-exact matches. Of the non-matched records, 3,633 (49.8%) were incidents where the person who recorded the address only listed the municipality, bridge, or street name ("Drug Street") with no house number. There were 7,744 (42.7%) addresses that were eligible to be re-matched (data not shown)

After the first round of geocoding, we reviewed the non-exact matches to ensure that the address was correctly matched. After re-matching the tied and unmatched observations, we gained an additional 2,847 (36.7%) matched records of 7,285 unmatched records. After this step, we matched these geocoded records to our cleaned, new database of 16,954 stamp bags from our first analysis for our subsequent mapping strategies. In our final mapping database, we had **4612 addresses (27.7%)** that could not be matched. This accounted for 4612 unique lab-tested items as well **as 3134 unique cases**, suggesting that much of what could not be mapped were single bag cases. The tables below show our final number of unique cases to be mapped and unique bags to be mapped.

Table 8: Frequency of Unique Cases and Bags to map, by drug, Allegheny County, 2010-2017

	Unique Cases (N, %)	Total Bags
Total	10610	16954
Heroin	9981 (94.1)	15756 (92.9)
Fentanyl	1121 (10.6)	1548 (9.1)
Fentanyl analogs	269 (2.5)	343 (2.0)
Cocaine	116 (1.1)	133 (0.8)

*Data from the Allegheny County Medical Examiner Office.
[1]Multiple cases can have multiple drugs; percent will not add up to 100.

Table 9: Unique cases that can and cannot be mapped due to missing information; Allegheny County, 2010-2017

	Total Unique Cases (N)	Mapped (N, %)	Not Mapped
Total	10610	7476 (72.3)	3134 (27.7)
Heroin	9981	7016 (70.3)	2965 (29.7)
Fentanyl	1121	791 (70.6)	330 (29.4)
Fentanyl analogs	269	204 (75.8)	65 (24.2)
Cocaine	116	86 (74.1)	30 (25.9)

*Data from the Allegheny County Medical Examiner Office.
[1]Multiple cases can have multiple drugs; percent will not add up to 100.

Table 10: Unique stamp bags that can and cannot be mapped due to missing information; Allegheny County, 2010-2017

	Total Unique Bags (N)	Mapped (N, %)	Not Mapped (N,%)
Total	16954	12342 (72.7)	4612 (27.3)
Heroin	15756	11471 (72.8)	4285 (27.2)
Fentanyl	1548	1119 (72.2)	429 (27.8)
Fentanyl analogs	343	260 (75.8)	83 (24.2)
Cocaine	133	100 (75.2)	33 (24.8)

*Data from the Allegheny County Medical Examiner Office.
[1]Multiple cases can have multiple drugs; percent will not add up to 100.

6.3.1.1 Descriptive: Submitting Agencies

The submitting agency field suggests where the stamp bags were seized regionally. Among all records, there were 137 distinct submitting law enforcement or other agencies that submitted stamp bag evidence. Among the instances where we could map the locations, there were 130 distinct agencies. Of these bags where the evidence that contained heroin, 129 distinct agencies submitted the evidence. Of the evidence that contained fentanyl, 94 distinct agencies submitted evidence. For fentanyl analogs, 48 distinct agencies submitted. For cocaine, 31 distinct agencies submitted evidence.

Among all records (whether they could be mapped or not), the leading agencies for submitting evidence were Pittsburgh PD – NV (1635), Pittsburgh PD Zone 1 (860), Pittsburgh PD Zone 3 (574), Allegheny County Police (530), Pittsburgh PD Zone 5 (488), Pittsburgh PD Zone 6 (436), Pittsburgh PD Zone 2 (390), Pittsburgh PD Zone4 (343), McKees Rocks PD (323), McKeesport PD (316), Wilkinsburg PD (304), Mount Oliver PD (299) and North Versailles (271).

6.3.1.2 Frequencies by Drug Type and Law Enforcement Agency (Data Not Shown)

The prior section lists the agencies that submitted the most seized evidence for testing. This next section evaluates what type of stamp bags that different agencies submitted, though it follows similar trends to the previous analysis. For heroin, the Pittsburgh City Police (all zones included), as well as McKees Rocks, McKeesport PD, Mount Oliver and Wilkinsburg frequently submitted evidence that contained the drug for testing. For fentanyl and fentanyl analogs, similar trends were seen except for Monroeville PD, which was one of the top ten most frequent agencies to submit evidence with it. For cocaine, there was far less evidence as compared to the opioids. We still saw similar trends though Pittsburgh police were not as frequent submitters.

6.3.2 Burden of Drug Activity: Thematic Mapping by Drug Type and Level of Sensitivity

One important caveat for thematic mapping is to note that, due to differences in numbers, the legend values are not the same across maps (or even within a sensitivity level). By selecting natural jenks, the software breaks data and makes a category where it would break naturally, which makes sense for data that is as variable as the stamp data. For the purposes of interpretation, a thick black border is shown on each map to show the boundaries of City of Pittsburgh.

The following map shows Allegheny County at the zip code level. The quantities of unique cases (or incidents), regardless of drug content, are displayed by zip code. We provide separate case maps for heroin, fentanyl, analogs and cocaine. In general, the largest "case load" is within the city limits of Pittsburgh, as well as the immediate outside municipalities. Similarly, many of the darkest shaded regions fall within the red boundary of Pittsburgh (but many also do not). Note that certain bags will no longer appear as the maps move from zip code to census tract to block group, as fewer and fewer have completed, detailed address information.

6.3.2.1 Stamp Bags (2010 and 2017, Heroin)

For heroin, we show two maps (2010 and 2017) to demonstrate any variation over time in quantity of cases by zip code. At the zip code level, this suggests that drug seizures with these drugs are fairly spread out across the county but have high burden within Pittsburgh. The maps for census tract and block group can be similar. Here, we show a selected number of results, given that they are purely descriptive.

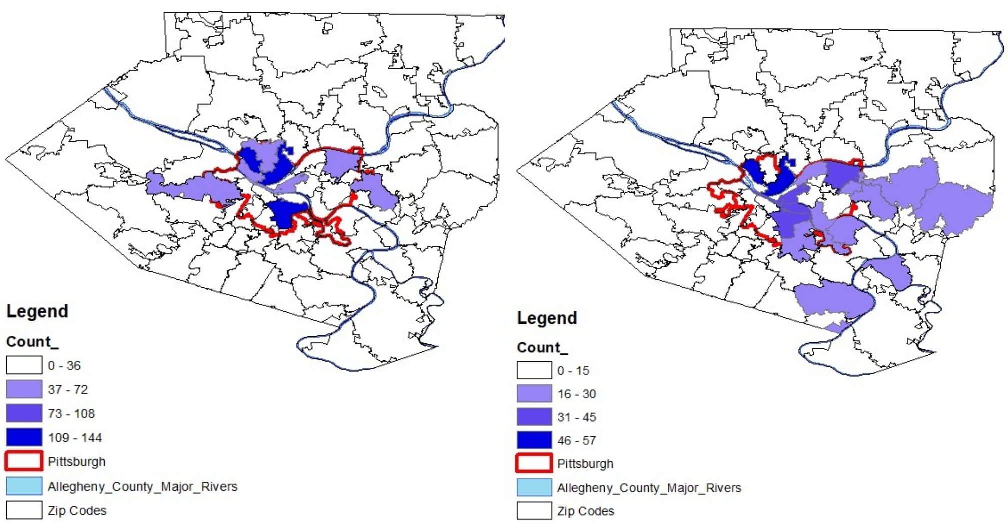

Figure 6: Heroin stamp bags by zip code, (2010 and 2017) Allegheny County, PA

6.3.2.2 Stamp Bags (2014-2017, Fentanyl)

Fentanyl has been mapped for the four years of data available (2014-2017). Fentanyl has a similar profile has heroin at the zip code, census tract and block group levels. As the number of stamp bags that contained fentanyl increased over time, the number of zip codes that had one or more bags with fentanyl increased (see Figure 9).

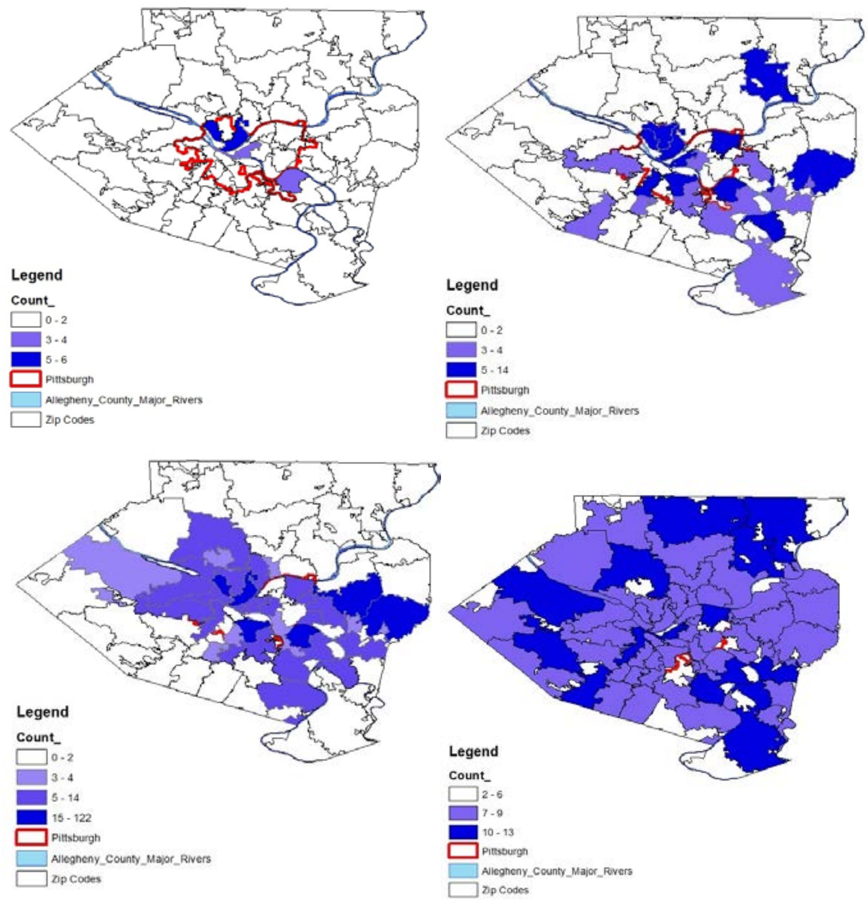

Figure 7: Fentanyl stamp bags by zip code; (top left: 2014, 2015, 2016, 2017), Allegheny County, PA

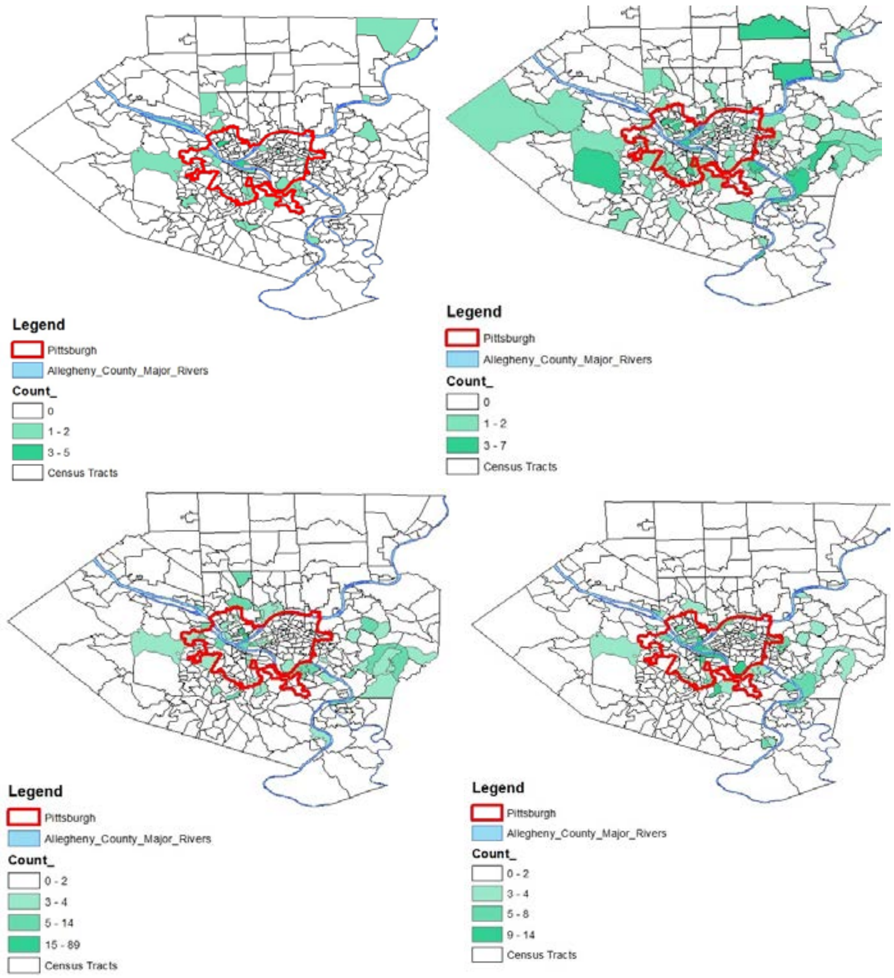

Figure 8: Fentanyl stamp bags by census tract (top left: 2014, 2015, 2016, 2017), Allegheny County, PA

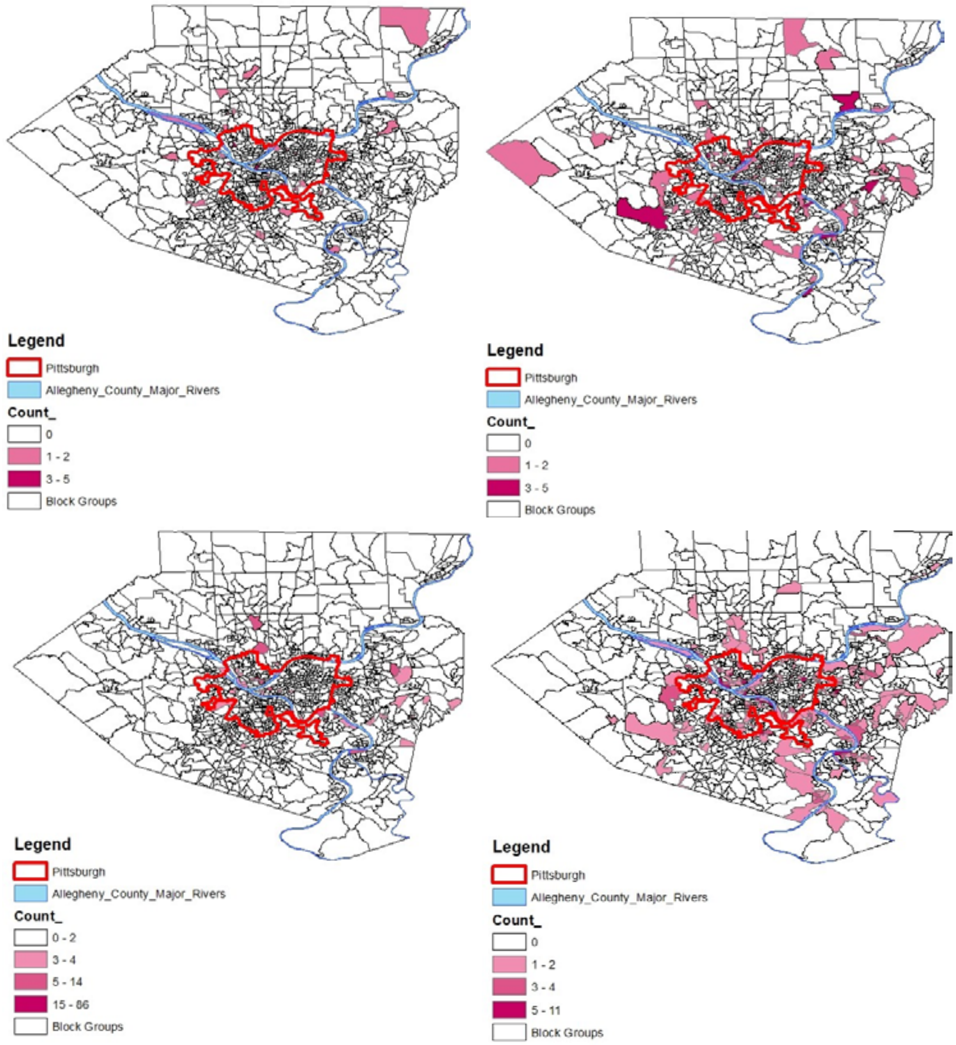

Figure 9: Fentanyl stamp bags by block group (top left: 2014, 2015, 2016, 2017), Allegheny County, PA

6.3.2.3 Stamp Bags (All Years, Fentanyl Analogs)

Fentanyl analogs have been mapped in the same way that cocaine has been mapped; the data years are aggregated to have better estimates by region. At the zip code level, fentanyl analogs look much the same way as heroin and fentanyl.

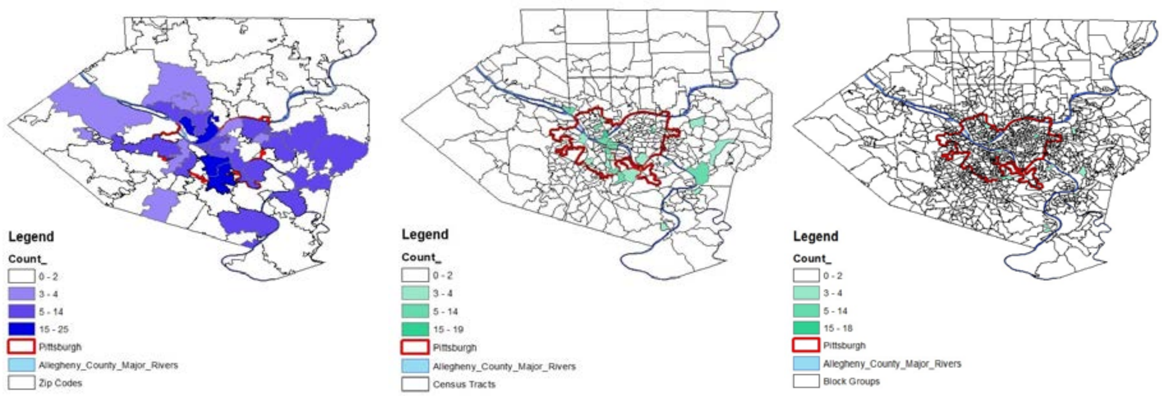

Figure 10: Fentanyl analog stamp bags by zip code, census tract, and block group years 2015-2017, Allegheny County, PA

6.3.2.4 Stamp Bags (All Years, Cocaine)

For cocaine, this map shows all years of data combined (2010-2017) to account for small quantities of bags. Note that the locations of stamp bags for cocaine are slightly different in some cases than heroin or fentanyl.

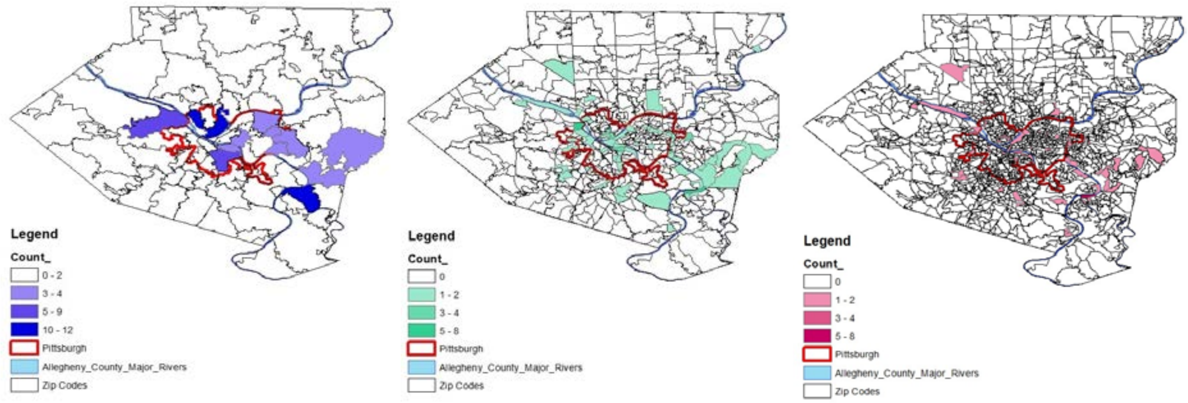

Figure 11: Cocaine stamp bags, by zip code, census tract, block group, years 2010-2017, Allegheny County PA

6.3.3 Cluster Analysis: Localized Hot Spots of Activity among Cases

The following maps display hot spot maps of the *unique cases* by drug type (heroin, fentanyl, fentanyl analog, and cocaine) for all years. Each dot represents a single case where that drug was recovered as part of the stamp bag evidence. Hot spots in this case represent areas with similar high numbers of cases where each drug was found present, indicative of drug activity in an area.

6.3.3.1 Cases (All Years, Heroin)

Among all three levels of hot spot analysis for cases where heroin was found in stamp bags, there were clear hot spots within the City of Pittsburgh and clear cold spots in areas such as the South Hills, Mount Lebanon, and Fox Chapel.

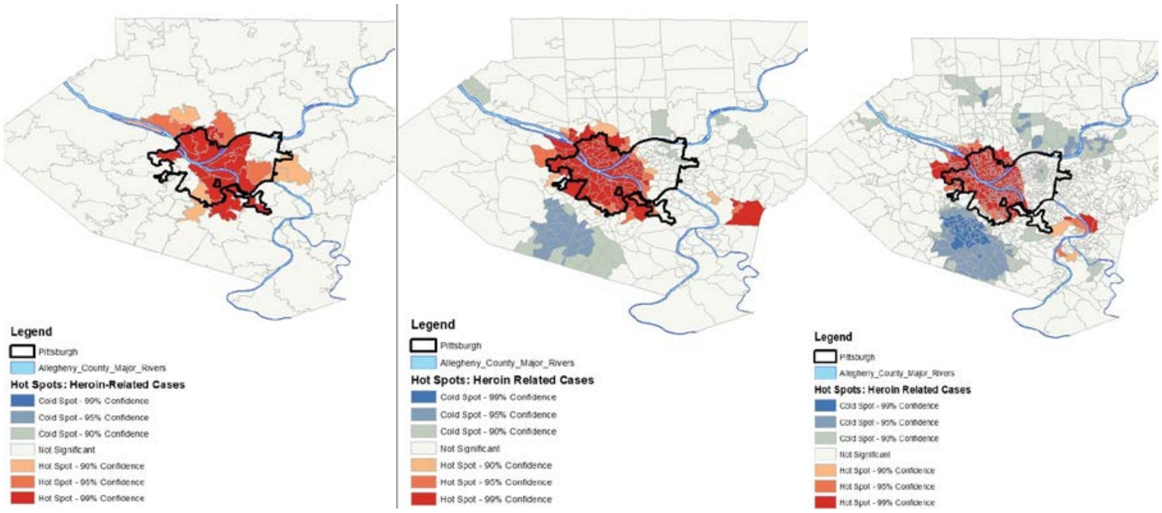

Figure 12: Hot Spot Analysis: Cases with Heroin Bags, zip code, census tract, block group, 2010-2017, Allegheny County, PA

6.3.3.2 Cases (All Years, Fentanyl)

For fentanyl cases, the patterns of hot spots mirrored those of heroin but showed more dispersion outside of the city. Significant cold spots were seen in both northern and southern areas of the city. Significant hot spots appeared for areas like Monroeville, which are to the east of the city. Interesting, activity in the eastern part of Pittsburgh was insignificant.

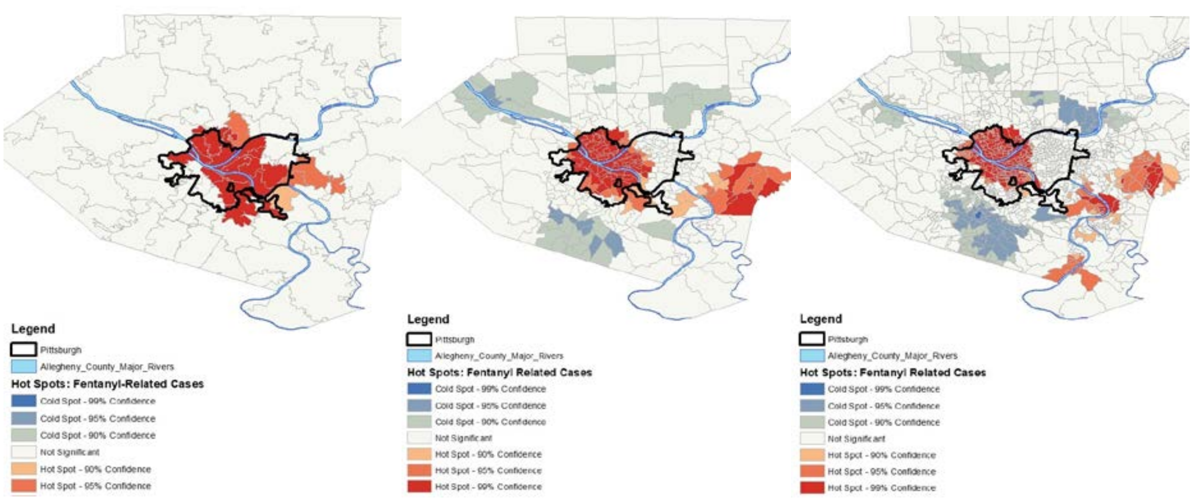

Figure 13: Hot Spot Analysis: Cases with fentanyl stamp bags (zip code, census tract, block group), 2014-2017, Allegheny County, PA

6.3.3.3 Cases (All Years, Fentanyl Analogs)

For fentanyl analog cases, the overall quantities were fewer, but similar hot spots remained. There were fewer significant spots that overlapped with fentanyl, but the cold spots were still south and north of the city. A small series of hot spots appeared in the lower part of the county, near Elizabeth and Jefferson townships.

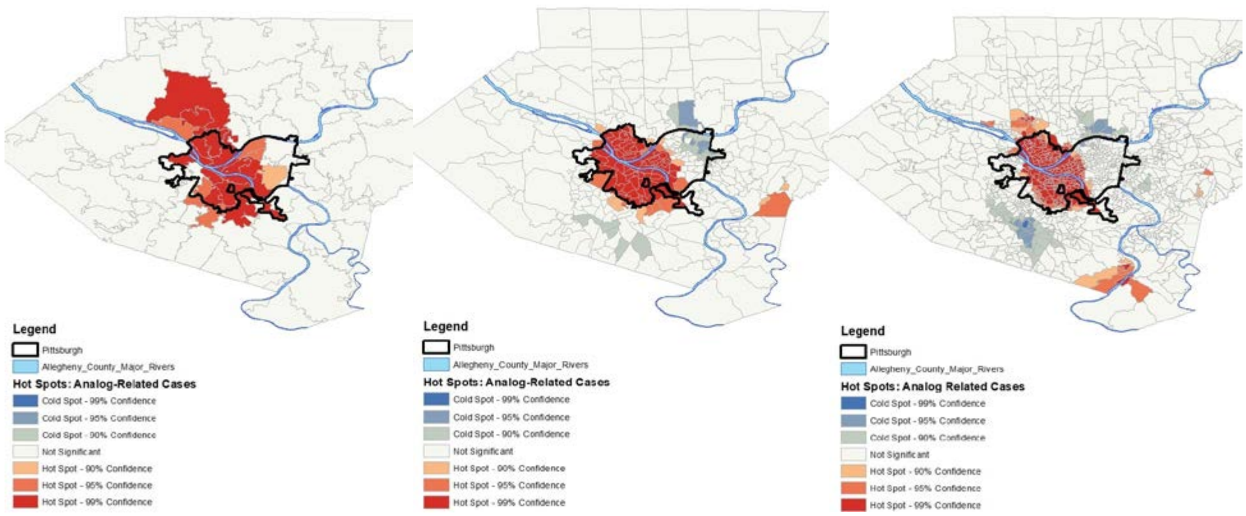

Figure 14: Hot Spot Analysis: Cases with fentanyl analog stamp bags (zip code, census tract, block group), 2015-2017, Allegheny County, PA

6.3.3.4 Cases (All Years, Cocaine)

Cocaine, unlike the opioids, had limited significant activity among its cases within the City of Pittsburgh. Even at the zip code level, it is evident that significant clustering is occurring in areas east of the city, such as McKeesport, McKees Rocks, and Monroeville.

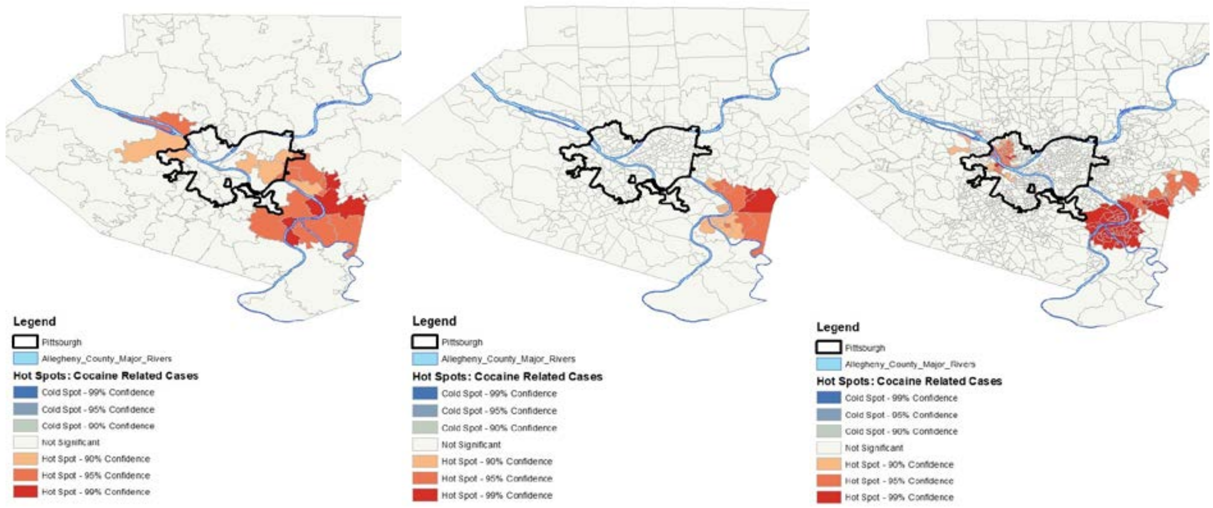

Figure 15: Hot Spot Analysis: Cases with cocaine stamp bags (zip code, census tract, block groups), 2010-2017, Allegheny County PA

6.4 DISCUSSION

6.4.1 Main Findings

There were four main parts to our spatial analyses. Overall, we could match over 70% of our original addresses after a two-step cleaning and re-matching process. Across drug types, similar numbers of cases and stamp bags were able to be mapped based on geocode results.

When we evaluated which law enforcement agencies were submitting evidence more frequently than others, we immediately could see a pattern emerge across all drugs. Pittsburgh City Police (all zones) frequently seized and submitted stamp bags for testing, as did McKeesport, McKees Rocks, Mount Oliver, North Versailles, and Monroeville. This could suggest a few things: 1) there are more people in these neighborhoods, 2) these areas are patrolled more often, and 3) there is more drug activity in these areas, regardless of whether residents are participating or not.

We created thematic maps by summarizing the number of drug-specific stamp bags at each geographic level. At the zip code level, the maps showed greater geographic range and spread where at least one bag occurred. At the census tract and zip code, fewer bags were able to be mapped, but there was also more heterogeneity. Much of the activity fell within the limits of Pittsburgh.

We tested three levels of geography for hot spot analysis: zip code, census tract, and block group. As our images show, the zip code level showed the least amount of detail and the least informative distributions. Using only the zip code level, we would assume that most of the stamp bag incidents cluster in the City of Pittsburgh and right beyond its borders for opioids, though the eastern part of the city had less activity. However, at the census tract and block group level, we see that many municipalities are experiencing the illicit opioid problem in that seizures are occurring in those areas. For cocaine, the eastern border of the state had significant clustering.

Cold spots occurred mostly to the north and south of the city and tended to fall in areas where the median income level was high. Examples include Dormont, South Hills, Fox Chapel and Mount Lebanon. These areas consistently appeared at the 90% and 99% confidence level, suggesting that these areas of low seizure activity did not occur by chance.

6.4.2 Strengths

This analysis is one of the first public health geographic analyses of stamp bags at the local level and is a timely and relevant evaluation for the ongoing epidemic. We had a large sample size with detailed address information that could be mapped at various sensitivity levels. Because the analysis was restricted to a small geographic area, we could plot a dot map that clearly showed areas of intense activity with proportional sizes to show repeated incidents. This was important because we wanted to differentiate between nearby places that were very different with respect to crime.

6.4.3 Limitations

There are caveats and limitations to these analyses. especially for purposes of interpretation. First, the database represents a sample of all stamped and unstamped bags that exist in the county. A sample of these bags are then tested, though this sample is likely to be representative of the bags that are recovered based on the sorting and testing methods employed by the drug chemistry unit. We cannot say for certain that the recovered stamp bags are representative of everything in the county since we do not have data on other types of drug evidence in this database.

Our results are most likely indicative of areas that have more people and more crime in general, as these areas tend to be lower-income, higher crime neighborhoods in the county. Without calculating rates or further adjusting for these factors, we cannot make valid comparisons between regions of the county with respect to illicit drug burden. Therefore, we comment on comparing years with natural jenks as the cutoff; natural cut points can change over time.

Second, we were limited in our ability to match our address list given the data we had. While we could ultimately match nearly three quarters of the addresses to x and y coordinates, we lost information for those where only a municipality or zip code was listed. These were geocoded to the central point of the polygon, which reduces the accuracy of our clustering analyses at finer levels (e.g. census tract and block group).

6.4.3.1 Misclassification Bias

While the data cleaning step recovered a tremendous amount of information, it is likely that there was some human error in classifying the address records. For the most part, the quality assurance steps will reduce this. Still, it is worthwhile to note that this massive quality assurance process will be more difficult to sustain or implement as part of the ongoing database updates and maintenance, and more streamlined methods might be a better approach.

6.4.3.2 Non-Causal Associations

Finally, we did not aim to answer the question of why certain stamp bags were clustering in specific geographic locations, nor did we attempt to account or explain these phenomena. Without mapping a relative value, such as a rate, we cannot truly compare different localities in terms of illicit drug “risk” or risk of exposure. In our results, the City of Pittsburgh appeared as a hot spot repeatedly. This could be attributed to the larger population in the city, or to the higher crime rates in the city. Our analyses were purely descriptive, but they were a first step in identifying patterns in illicit drug evidence that could be useful for resource planning, enforcement, and public health outreach. In addition, our methods can be adapted (much like those of alcohol and other drug literature) to different types of illicit drugs.

6.4.4 Additions to the Literature

Stamp bag data is a unique form of illicit drug evidence that, while not necessarily common across the United States, can be used as an example of one new approach to monitoring illicit drug trends. Our analyses are one of the first in peer-review public health literature using illicit drug evidence as the unit of analysis and can be adapted for other types of illicit drug evidence.

7.0 DETECTING THE RAPID INCREASE IN ILLICIT FENTANYL IN ALLEGHENY COUNTY, PA

A version of this aim was published prior to completion of the dissertation in *Public Health Report.* (91)

7.1 INTRODUCTION

The number of fatal opioid overdoses in the United States quadrupled from 8050 in 1999 to 33 091 in 2015. (103) Major contributors to these deaths have been heroin and synthetic opioids, especially fentanyl, a legal Schedule II substance that is 20 to 50 times more potent than heroin, (99, 182) and its analog, acetyl fentanyl, which is 80 to 100 times more potent than morphine and 5 to 15 times more potent than heroin.(112-114) To quantify, deaths specifically involving synthetic opioids such as fentanyl increased from 3105 in 2013 to nearly 20 000 in 2016. (183) Clusters of deaths have resulted from heroin adulterated with fentanyl or acetyl fentanyl in the United States. (112, 113, 117, 183-184) The role of these drugs in US overdose deaths is increasing. Heroin prices have remained low since the late 1990s, and heroin has become more available than before. Fentanyl has increasingly been packaged with heroin, or even manufactured as counterfeit pills out of clandestine laboratories. (117) Fentanyl is marketed under a number of names and can also be prescribed legally for pain. For the purposes of this report, we focus on illicit fentanyl. (185)

Information on the circulation and use of these drugs, and the resultant mortality, comes from two government sources: public health and law enforcement. Public health information comes from the investigation of overdose deaths, such as death certificate information and toxicology data from medical examiners' or coroners' offices, which identify the specific drugs that contribute to individual overdose deaths. By monitoring these data over time, public health authorities can identify trends in the types of drugs that are contributing to these deaths and report on them. (9, 78, 103, 183) However, public health surveillance systems do not have a way to rapidly capture data on the use and circulation of fentanyl and its analogs. In 2015, for example, 17% of death certificates did not identify specific drugs involved in overdose deaths. (9)

Law enforcement authorities use other systems to monitor trends in illegal drug circulation. One is the monitoring of drugs seized by law enforcement authorities. (124, 145, 185) At the national level, the National Forensic Laboratory Information System (NFLIS) tracks trends in the circulation of illegal drugs. One report found a 426% increase in fentanyl submissions by the US Drug Enforcement Administration and law enforcement into NFLIS, from 1015 fentanyl submissions in 2013 to 5343 fentanyl submissions in 2014. This same study found that fentanyl deaths were fueling deaths from synthetic opioids. (118)

In Pennsylvania, fentanyl has gradually replaced heroin as the drug that contributes the most to these deaths. In 2015, the most common drugs in fatal overdoses were heroin and fentanyl. (116) In Allegheny County, Pennsylvania, 1053 of 3374 (31.2%) people who died of a drug overdose between 2008 and 2017 had fentanyl in their bodies as evidenced by toxicology. (50)

In Pennsylvania and other surrounding regions in the Northeastern United States, small wax packages called stamp bags are used for illicit drug sales. The word “stamp” refers to the graphic logo sometimes placed on the wax bag by drug dealers to show the contents or origin of the bag. Stamp bags are recovered during undercover purchases, drug seizures, or seizures at the scene of a fatal or nonfatal overdose. In Allegheny County, Pennsylvania, roughly 1000 unique stamps were found among stamp bags collected as drug evidence in 2016 (data not shown). Stamp bags in Allegheny County contain powdered drugs (not pills or patches), often with bulking agents or other drugs. For example, heroin may be found mixed with cocaine or methamphetamine.

We studied the number and percentage of laboratory-tested, seized stamp bags containing fentanyl, fentanyl analogs, and heroin in Allegheny County from 2010 through 2017 and explored the value of using stamp bags to monitor trends in the circulation of these drugs locally.

Figure 16: Example of recovered stamp bags as part of drug evidence in Allegheny County, Pennsylvania, 2010-2016
Stamp bags are small wax packets that contain mixtures of drugs, most commonly heroin, that are often seized by law enforcement officers and retained as legal evidence. Laboratory-tested bags in this study all had a stamp. Unstamped bags were not included in this analysis. Figure was obtained with permission from the Allegheny County Medical Examiner Office and *Public Health Reports*.

7.2 METHODOLOGY

7.2.1 Data Sources

We compiled laboratory test results and stamp names of stamp bags from the drug chemistry laboratory of the Allegheny County Office of the County Medical Examiner (OCME) in Pittsburgh, Pennsylvania. All stamp bags in the database were seized as evidence by law enforcement authorities. Drug evidence must be submitted for testing by using proper protocols described in the evidence submission manual. (149) If an agency suspects that a stamp bag contains a certain drug, the name of the drug should be specified upon submission. Only stamp bags that are linked to an open, active law enforcement case are tested. Drug chemistry testing is performed exclusively in the Allegheny County Drug Chemistry laboratory of the OCME. Our analysis did not include toxicology from human samples; as such, it was expedited and approved by the University of Pittsburgh Institutional Review Board.

7.2.2 Sampling

Seized stamp bags can be single bags or large batches of bags. At the laboratory, technicians sort through the batch obtained by a seizure. Bags in a batch are initially sub-itemized by stamp, color, and other characteristics (e.g., suspected drug). A single batch of stamp bags could contain two or more groups (e.g., one group of white powder bags with a unique stamp, one group of brownish powder with a unique stamp). Because of resource constraints, not all bags are tested. A single bag is randomly selected from each group of bags and tested by a technician. Gas chromatography–mass spectroscopy is used to confirm the identity of any controlled substances that are present. See Chapter 5.0 for more detailed explanations of the sampling and testing.

7.2.3 Dataset

We used a dataset consisting of drug chemistry results of stamp bags that were tested in the laboratory from 2010 through 2017. We grouped the types of drugs found in the bags into the following 6 categories, which are not mutually exclusive: (1) any heroin (presence of any heroin or heroin hydrochloride, with or without other drugs); (2) heroin alone (heroin was the only controlled substance present; other nondrug substances may have been used to bulk or dilute in the bag, but no other drugs were present); (3) any fentanyl (any fentanyl was present; analogs may have been present but were not counted as fentanyl, with or without drugs); (4) fentanyl alone (fentanyl was the only controlled substance present; other nondrug substances may have been used to bulk or dilute in the bag, but no other drugs were present); (5) heroin and fentanyl with or without other drugs, (6) cocaine or cocaine with fentanyl, with or without other drugs, and (7) any fentanyl analogs (acetyl fentanyl, acryl fentanyl, furanyl fentanyl, benzyl fentanyl, butyryl fentanyl, 4-methoxy butyryl fentanyl, methoxyacetyl fentanyl, p-fluoroisobutyryl fentanyl (PFBP), trans-3-methylfentanyl, cis-3-methylfentanyl, cyclopropyl fentanyl, carfentanil, phenyl fentanyl, U-47700, and valeryl fentanyl with or without other drugs). Fentanyl analogs were not categorized as fentanyl and do not necessarily appear in bags with fentanyl. These groups are not mutually exclusive; the use of "any" fentanyl, for example, means that other drugs could be present in stamp bags including fentanyl analogs. We calculated descriptive statistics of these bags by drug and year of analysis by using Microsoft Excel and SAS. (151)

As a note, the published analysis in *Public Health Reports* was performed from the perspective of the drug chemistry unit and their testing capabilities for data years 2010 through 2016. (91) Rather than evaluating the date that the drugs were seized (and therefore the yearly burden of the drugs) as was done in the two previous aims, we used the date of analysis to determine *when the drugs were detected*. Therefore, the proportions of drugs by year will be different if compared to the published version as well as the drug definitions. Fewer fentanyl analogs were included in that analysis given the newly detected analogs in 2017. In addition, we did not exclude cases from outside of the county because we were interested in how much of each drug the unit detected. This is not reflective of the true burden found in the county in real-time, which will be reported here.

In addition, we added additional drug categories to include any cocaine, with or without other drugs and cocaine and fentanyl, with or without other drugs for the dissertation purposes. Our published version was limited to 2016 data, but we expanded the analysis to include 2017 upon availability and updated our estimates.

7.2.4 Supplemental Analyses

As additional analyses for the aim, we reported the proportion of stamp bags where specific fentanyl analogs were detected by year. This demonstrated the fluctuation in various drugs on the streets that we detected in near real-time We also reported the stamps that were found on fentanyl and fentanyl analog bags each year and report the five most common stamps found on these bags each year. Instances where six or more stamps were tied are suppressed. Full lists of stamps are not included but may be made available.

7.3 RESULTS

7.3.1 Fentanyl

The laboratory tested 16,954 stamp bags from 2010 through 2017, of which 15,756 (92.9%) contained any heroin, 14666 (86.5%) contained heroin alone, 1,548 (9.1%) contained any fentanyl, 626 (3.7%) contained fentanyl alone, 133 (0.8%) contained any cocaine, 31 (0.2%)

contained cocaine and fentanyl, 800 (4.7%) contained heroin and fentanyl, and 343 (2.0%) contained fentanyl analogs. The proportion of heroin declined over time, while the proportion of fentanyl and fentanyl as the only drug present increased sharply after 2014.

Table 11: Number and percentage of laboratory-tested stamp bags that contained heroin, fentanyl, or fentanyl analogs, Allegheny County, Pennsylvania, 2010-2017

N (%)	**Total (n=16954)**	**2010 (n=1712)**	**2011 (n=1314)**	**2012 (n=1503)**	**2013 (n=2321)**	**2014 (n=2885)**	**2015 (n=3037)**	**2016 (n=2777)**	**2017 (n=1405)**
Heroin	15756 (92.9)	1663 (97.1)	1283 (97.6)	1469 (97.7)	2277 (98.1)	2813 (97.5)	2912 (95.9)	2440 (87.8)	899 (64.0)
Heroin alone	14666 (86.5)	1652 (96.4)	1276 (97.1)	1459 (97.1)	2267 (97.7)	2742 (95.0)	2688 (88.5)	1999 (72.0)	583 (41.5)
Heroin and fentanyl	800 (4.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	50 (1.7)	163 (5.3)	375 (13.5)	212 (15.1)
Fentanyl	1548 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	59 (2.0)	237 (7.8)	641 (23.1)	610 (43.4)
Fentanyl alone	626 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	9 (0.3)	63 (2.1)	245 (8.8)	309 (21.9)
Fentanyl Analogs	343 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	57 (1.9)	49 (1.8)	237 (16.8)
Cocaine	133 (0.8)	11 (0.6)	7 (0.5)	7 (0.4)	8 (0.3)	9 (0.3)	19 (0.6)	42 (1.5)	29 (2.0)
Cocaine alone	7 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	1 (0.0)	4 (0.1)	1 (0.0)
Cocaine and fentanyl	31 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5(0.2)	11 (0.4)	15 (1.1)

*Data from the Allegheny County Medical Examiner Office.[1]Stamp bags are small wax packets that contain mixtures of drugs, most commonly heroin, that are often seized by law enforcement officers and retained as legal evidence.
[2]Laboratory-tested bags in this study all had a stamp.
[3]Any fentanyl indicates any fentanyl was present; analogs may have been present but were not counted as fentanyl, with or without drugs. Fentanyl alone indicates fentanyl was the only controlled substance present; other nondrug substances may have been used to bulk or dilute in the bag, but no other drugs were present. Fentanyl analogs indicates the presence of acetyl fentanyl, butyryl fentanyl, furanyl fentanyl, cyclopropyl fentanyl, 4-methoxy butyryl fentanyl, trans-3-methylfentanyl, cis-3-methylfentanyl, carfentanil and other analogs, with or without other drugs.
[4]Numbers for this analysis will differ from publication given different date used to analyze findings.

The proportion of tested bags that were detected by the unit containing fentanyl or its analogs increased from 2010 to 2017. By 2017, fentanyl was found in forty-three percent of tested bags that were seized in 2017, and 309 (21.9%) tested bags contained fentanyl alone in 2017. Fentanyl analogs did not appear in stamp bags until 2015 (57/3037) tested bags in that year, but the presence of fentanyl analogs increased to 237 (16.8%) tested bags in 2017.

7.3.2 Detection of Synthetic Opioids (Timeliness)

Counts and percentages of fentanyl analogs and other synthetic opioids (excluding fentanyl) detected in tested stamp bags were broken out by year from 2015 through 2017 (see counts and proportions in the table below). Each proportion represents the total percentage of bags where that drug was detected. It is common with these drugs to find multiple analogs in a single bag, so a bag may be counted more than once in this table and will not add up to the total number of bags containing any analog or synthetic opioid.

Clearly, fentanyl was present in stamp bags as early as 2014 and rapidly increased as a present drug over time. In contrast, the fentanyl analogs were relatively infrequent in stamp bags, though some drugs were more prevalent than others. In 2015, acetyl fentanyl was the only fentanyl analog that was found in seized and tested bags (56; 1.8%). In 2016, furanyl fentanyl (15; 0.5%) appeared in the sampled and tested bags, as well as U-47700 (6; 0.2%). In 2017, the proportion of bags where furanyl fentanyl (68; 4.8%) and U-47700 (39; 2.8%) were detected increased. Several fentanyl analogs appeared for the first time in 2017, including cyclopropyl fentanyl (23; 1.6%) and methoxyacetyl fentanyl (10; 0.7%). Acetyl fentanyl appeared in 10 bags (0.7%)

Table 12: Percent of instances where specific, select synthetic opioids were detected in laboratory-tested stamp bags by year of seizure. Allegheny County, Pennsylvania, United States; 2014-2017

Synthetic Opioid	**4 Year Total (10104)**	**2014 (n=2885)**	**2015 (n=3037)**	**2016 (n=2777)**	**2017 (n=1405)**
Fentanyl	1547 (15.3)	59 (2.0)	237 (7.8)	641 (23.1)	610 (43.4)
Acetyl fentanyl	83 (0.8)	0 (0.0)	56 (1.8)	17 (0.6)	10 (0.7)
Benzyl fentanyl	2 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)
Butyryl fentanyl	39 (0.4)	0 (0.0)	1 (0.0)	0 (0.0)	38 (2.7)
Carfentanil	7 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	6 (0.4)
Cyclopropyl fentanyl	23 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	23 (1.6)
Furanyl fentanyl	83 (0.8)	0 (0.0)	0 (0.0)	15 (0.5)	68 (4.8)
Cis-3-methylfentanyl	8 (0.1)	0 (0.0)	0 (0.0)	7 (0.2)	1 (0.0)
Trans-3-methyl fentanyl	7 (0.0)	0 (0.0)	0 (0.0)	7 (0.2)	0 (0.0)
Methoxyacetyl fentanyl	10 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	10 (0.7)
PFBF	77 (0.8)	0 (0.0)	0 (0.0)	4 (0.1)	73 (5.2)
Phenyl fentanyl	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)
Valeryl fentanyl	2 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)
U-47700	45 (0.4)	0 (0.0)	0 (0.0)	6 (0.2)	39 (2.8)

*Data from the Allegheny County Medical Examiner Office.

[1]Other drugs may be present in the tested bags where synthetic opioids were found. These counts do not represent individual bags, necessarily.

[2]Prior to 2014, the stamp bags that were seized and tested did not contain other synthetic opioids.

[3]Para-fluoroisobutyrylfentanyl

7.3.3 Exploratory Results: Fentanyl Stamps

The following Table shows the total number of unique stamps among stamp bags that were seized and ultimately tested in our final database. From 2010 through 2017, there were 3790 unique stamps (as determined by exact matching name or description). This suggests that stamps repeatedly show up across time, even if drug contents or dealers change.

Table 13: Frequency of Unique Stamps on stamp bags recovered and tested, Allegheny County Medical Examiner Office, 2010-2017*

Year	2010	2011	2012	2013	2014	2015	2016	2017
Count	570	532	659	769	880	892	969	640[1]

*Data from the Allegheny County Medical Examiner Office.
[1]Drop may be attributed to lags in data processing and entry for the end of year
[2]Photographic evidence was not used/available to discern differences in stamps.

Table 14: Frequency of Unique Stamps found on recovered stamp bags, by drug and year, Allegheny County, 2010-2017

Year	2010	2011	2012	2013	2014	2015	2016	2017
Heroin	553	518	642	754	860	871	871	436[1]
Fentanyl				1	21	90	256	325
Cocaine	9	7	7	6	7	16	35	24
Analogs						28	36	140

*Data from the Allegheny County Medical Examiner Office.
[1]Drop may be attributed to lags in data processing and entry for the end of year
[2]Multiple drugs can occur in the same bag, so the unique stamps may appear across several drugs.
[3]Photographic evidence was not used/available to discern differences in stamps.

Table 15: Top 5 Stamps found on stamp bags with fentanyl, by number of bags and by year, Allegheny County, PA: 2013-2017

Name (N)	**2014**	**2015**	**2016**	**2017**
Rank 1	Theraflu (23)	Jaguar (14)	Obsession (42)	Spider (11)
Rank 2	Bud Ice (12)	Predator (13)	Jason Bourne (23)	Call of Duty (10) Ferrari (10) Pepsi (10)
Rank 3	Next Adventure (3) Safe House (3)	Oliver Queen (11)	Tuff Stuff (18)	A+ (8) Get Out (8) Cobra (8)
Rank 4	More than six stamps (1)[1]	New Arrival (9)	CEO (15)	New Arrival (7) Scorpion (7) The King (7)
Rank 5		Beast Mode (7) Super (7)	Peace of Mind (11)	More than six stamps (6)

*Data from the Allegheny County Medical Examiner Office.
[1]If more than six stamps had the same frequency, then they were not reported.

7.3.4 Exploratory Results: Fentanyl Analog Stamps

Due to the sheer number of stamps found each year on stamp bags, we limited our reporting to stamps found on bags that contained fentanyl and fentanyl analogs. The following tables list the most commonly found stamps by year for 2015 through 2017 based on text descriptions of the stamps for fentanyl analogs. No photographic evidence is available. Ties are listed.

Table 16: Top 5 Stamps found on stamp bags with fentanyl analogs or U-47700, by number of bags and year, Allegheny County, PA: 2015-2017

Name (N)	2015	2016	2017
Rank 1	Flatline (6)	Money Bags (4)	Frank Lucas (13)
Rank 2	Diesel (5)	Spicy (3)	Louis Vuitton (11)
Rank 3	Road Rage (4) Skull Candy (4)	More than six stamps (2)[1]	XXX (8)
Rank 4	Call of Duty (3) Dragon (3) Oliver Queen (3) UPS (3) Dinosaurs (3)		Ferrai (6)
Rank 5	Do Not Enter (2) Rolex (2) SuperMan (2) Dinosaur (2)		Spider (5)

*Data from the Allegheny County Medical Examiner Office.
[1]If more than six stamps had the same frequency, then they were not reported.

7.4 DISCUSSION

7.4.1 Main Findings

To our knowledge, this is the first public health analysis to describe stamp bag contents and track changes in the presence of illicit fentanyl. Although the proportion of stamp bags that tested positive for heroin in Allegheny County was relatively stable from 2010 to 2017, the number of stamp bags that tested positive for both heroin and fentanyl, fentanyl alone, or any fentanyl analogs increased. The combination of heroin and fentanyl in stamp bags did not exist in 2010, but this combination accounted for 15.1% of bags by 2017. This finding is consistent with local and national reports of drug activity during the past few years. (53, 109, 117, 153, 183, 187)

Monitoring drug evidence can provide data on drugs in circulation that may not be available from typical public health surveillance systems, such as drug overdose mortality and toxicology data from medical examiners' or coroners' offices. Mortality data lag about 18 months. Also, many opioids are combined into groups for International Classification of Diseases, Tenth Revision, reporting, which results in lost information about opioid deaths. (7) Drug evidence data are usually available more quickly than public health data. In Allegheny County, drug evidence data for stamp bags seized during 2017 were already processed and available.

Unlike toxicology data from medical examiners’ or coroners’ offices, data from drug evidence can provide information on many unique drugs in their original chemical form, before they are metabolized in the body. Some potentially dangerous drugs, such as U-47700 (144), are not always identified in the toxicology testing process or are not reported on the death certificate. Although toxicology testing is an excellent tool, the detection of opioids and their analogs can be difficult, depending on which assay or test is used and how the results are interpreted. For example, synthetic opioids are not detected by some commercial serum assays and urine testing. (188) Chemical testing of the drugs using mass spectrometry, on the other hand, can identify a wider range of substances. New “peaks” can be identified easily, which can represent new and unusual drugs or compounds. (189)

7.4.2 Limitations

This study had several limitations. First, these findings represent a sample of all stamp bags submitted to the laboratory; the total quantity of bags submitted to the laboratory was not recorded until 2015 and, therefore, was not available. Every stamp bag cannot be tested. Bags that were linked to active law enforcement cases were prioritized, meaning that bags were not tested if criminal charges were not filed. In addition, we did not report on other substances found in the bags beyond fentanyl and its analogs, which could be important for identifying other drugs of concern.

For this analysis, we chose to analyze the stamp bag evidence from the perspective of the completion data for chemical testing. This data does not indicate the exact time when the drugs were present on the street as there is a lag between the time they are picked up off the street and the time they are analyzed in the lab. However, this still indicates the timeliness of this process and the ability to detect these drugs in near-real time. Refer to Chapter 5.0 for a more detailed list of limitations that apply to this analysis as well.

7.4.3 Additions to the Literature

Stamp bags can provide valuable insight into the illegal drug trade. A stamp bag monitoring system can serve as a complementary form of surveillance for other public health and law enforcement systems. For example, stamp bag data can be combined with prescription drug monitoring and mortality data to answer questions about how and where people are seeking drugs. In addition, these data are available in near-real time and can serve as an early warning of illegal drugs that are currently available for purchase and used at the local level. Although this brief report describes drugs found in stamp bags, data on other drug evidence can provide information about other trends in illicit drug use (e.g., illegal pills). The methodology for examining drug evidence can be explored and expanded for public health across the United States. Law enforcement and public health officials might consider how data on drug evidence can inform educational campaigns, resource allocation, and prevention strategies. First responders can benefit from information on drugs in circulation and can also be prepared with naloxone in the event of overdose.

8.0 SUMMARY OF FINDINGS AND RECOMMENDATIONS

The final chapter of this dissertation summarizes 1) the specific aims and overall objectives, 2) the key elements of the methodology, 3) the main findings, 4) the major limitations of the dataset and the analyses, and 5) recommendations and future areas for research.

8.1 REVIEW OF AIMS AND OBJECTIVES

The purpose of this dissertation was to acquire and use a non-traditional public health dataset to address timely and relevant public health questions related to the local drug overdose problem. We focused on the illicit drug supply in Allegheny County, Pennsylvania using a surveillance database. Below are the specific aims:

Aim 1: Develop an illicit drug surveillance system for use by public health, law enforcement, and the ME by merging data sources from law enforcement and drug chemistry for incidents of stamp bag seizures

- Create and standardize drug category definitions for monitoring illicit drugs in stamp bags
- Develop a sustainable infrastructure and process for adding future years of data
- Develop quality control checks for ensuring accuracy of matching, cleaning and measurement

- Create and implement rules for data cleaning, particularly to clean and/or remove duplicate observations and to exclude irrelevant observations
- Describe characteristics of the database, including population characteristics and stamp bag drug contents

Aim 2: Identify spatial patterns among stamp bag seizures in Allegheny County, PA from 2010 through 2017 using the surveillance database

- Geocode addresses using a two-variable matching algorithm to ensure completeness of the data
- Describe the results of geocoding processes.
- Create thematic maps to describe the overall burden by geographic region of stamp bags, as well as differences using hot spot mapping.

Aim 3: Describe the increase in illicitly manufactured fentanyl in Allegheny County, PA using stamp bag data.

- Describe the change in fentanyl that is detected within stamp bags over time, as well as combinations of fentanyl with other drugs
- Identify specific, unique fentanyl analogs that have been detected in the county since 2014
- Report the stamps that are associated with fentanyl and fentanyl analog stamp bags

8.2 REVIEW OF METHODOLOGY

8.2.1 Methods: Aim 1

The following methods were used in this dissertation to analyze and quantify illicit opioids in Allegheny County, and begin to identify patterns among stamp bags. First, we built a database of stamp bag seizures in Allegheny County, PA from 2010 through 2017. Using this database, we identified all unique individuals associated with the seizures and described the demographic characteristics for these individuals, including aggregate measures for age, race, and sex. We calculated the proportion of stamp bags that contained any mention of specific drugs, using pre-defined categories that we used after consulting the literature. Finally, we turned the database over to the drug chemistry unit for future analyses, as well as detailed instructions and procedural information for replicating the process for additional data years. Because the analyses were done using SAS (151), pieces of the project were completed and tested using Excel to allow for an easier transition back to the medical examiner office.

8.2.2 Methods: Aim 2

For our second aim, we geocoded all available street addresses where stamp bag seizures occurred between 2010 through 2017 and eliminated incidents where no information was available, addresses could not be matched, or cases occurred outside of the county. We calculated measures of spatial autocorrelation at the block group, census tract and zip code level across years. We performed these analyses for heroin, cocaine and synthetic opioids for unique cases.

8.2.3 Methods: Aim 3

For our final aim, we created distinct definitions for reporting fentanyl and heroin combinations from stamp bags and calculated the proportion of stamp bags where these combinations were found using the drug chemistry database (while we published a report using the lab test completion date as our guide, we revised the dissertation analyses to match our first aim and to evaluate the burden in the community rather than the testing capability of the lab). We reported specific analogs that were detected in stamp bags and reported the most common stamps that were marked on the bags for fentanyl and fentanyl analogs.

8.3 REVIEW OF FINDINGS

8.3.1 Aim 1

The findings of this dissertation can be summarized by aim in previous chapters, but here we describe the overall findings and how they relate. The demographic characteristics of individuals associated with these incidents are like those of a typical heroin user (47) though we did not analyze seizures with and without heroin separately. Most individuals were male and white, and the median age was 28 years. The drug contents of stamp bags have changed from 2010 through 2017, though the clear majority still contain heroin. However, we documented a steep increase in fentanyl and its analogs after 2014.

8.3.2 Aim 2

Overall, we generally found good data quality with respect to data cleanliness and ability to geocode. Still, we matched less than 80% of our original records. The burden of incidents where stamp bags are recovered and tested is unevenly distributed across Allegheny County. When we performed hot spot analysis, we could see evidence of highly intense clustering, or “hot spots”, across all drugs, years, and levels. Similarly, we could identify some areas as “cold” spots where there were values far below the mean. Unsurprisingly, the City of Pittsburgh was a common hot spot for cases where stamp bags with opioids were found. Cocaine, on the other hand, tended to be recovered in areas outside of the city of Pittsburgh.

8.3.3 Aim 3

We found that the drug contents of stamp bags have changed over time in Allegheny County, Pennsylvania. The proportion of stamp bags that contain illicit fentanyl and fentanyl analogs has increased between 2010 through 2017, with the most drastic increases after 2014. While acetyl fentanyl was the first fentanyl analog to appear in the county in 2015, many new analogs have been detected in the bags since then.

8.4 REVIEW OF LIMITATIONS

As previously described, the medical examiner drug chemistry data was not designed to be collected for the purposes of public health surveillance and monitoring. Therefore, it is important to evaluate the limitations of this data, its collection procedures, and its generalizability to other jurisdictions. For reference, our process schematic is shown below in **Section 8.4.1.**

8.4.1 Sources of Bias

There are several sources of possible bias that could affect our estimates and overall statistics; most of this bias likely occurs during the data collection and sampling procedures (which is a function of limited time and resources for the participating agencies). Apart from that, there are significant resource limitations of time, staffing, and funding. The following sub-sections explain each possible source and how it might affect the results.

8.4.1.1 Representativeness of Data

Law enforcement have limited time and staff to patrol all geographic regions for drug-related activity, and therefore the bags they collect are a sample. We assume that the stamp bags that are recovered by police are representative of the entire "population" of stamped bags that exist in the county, and therefore the individuals associated with these incidents are representative of all individuals who are participating in the local illicit drug trade and use. Unfortunately, we cannot account for "unstamped" bags that exist in the county with our database. There are unstamped wax bags that are seized by law enforcement and submitted for testing; however, current data entry methods and limited staff time do not allow us to differentiate these bags from other types of drug evidence. In part, it is a function of how the data are recorded and flagged in the internal databases. Therefore, we could not differentiate a plastic bag containing heroin from an unstamped wax bag containing heroin from a pill bottle containing heroin in the raw drug evidence data.

As a result, we do not assume that our stamped bags are representative of ALL drug evidence in the county, especially counterfeit pills. The DEA has reported that illicit fentanyl and other illicit drugs have been incorporated into counterfeit pills using pill presses (190) as of 2014, which is something we cannot account for with our data at this time.

8.4.1.2 Sampling Bias

A major consideration is the effect of police activity and socioeconomic factors on our findings, which are not controlled for in our analyses since they are descriptive. There is a growing body of evidence that suggests arrests for crime and drug-related activity are associated with both geographic-level income inequality and racial bias on the part of law enforcement (191-193). Given the stark differences in median income levels and population demographics across Pittsburgh neighborhoods, it is reasonable to assume that specific population subgroups are less likely to encounter law enforcement based on where they live, such as higher income, primarily white populations. (194-195) Our results demonstrated that the same neighborhoods were consistent "hot spots" of drug activity; most were of low socioeconomic status. Individuals in low-income, urban neighborhoods are more likely to encounter opportunities to purchase illicit drugs (196-197) even though they may not have significantly higher drug use (198). This could be a function of the visibility of drug activity, which tends to be greater in black urban neighborhoods (198) Private drug dealings occur in more clandestine areas and are often unknown to police, and sellers and buyers increasingly attempt to hide dealings. (199-200) Sampling can also be affected by how aggressively law enforcement officials pursue criminal charges. In a survey of more than 200 non-violent offenders in New Haven, Connecticut, blacks and whites reported similar drug dealing activity, yet blacks tended to have more severe criminal charges. (201)

It makes sense that these issues would affect who ends up in our database and which neighborhoods light up as hot spots, but it is less likely that this bias would affect the overall proportion of seized and tested bags that contain heroin, fentanyl, and cocaine. We would not expect the overall proportion of bags with heroin to change dramatically regardless of where the bags are being seized from because it is a function of the larger heroin market. Further, a review of drug network characteristics stated that various legal and enforcement activities rarely affect overall patterns of illicit drug production, sales, or use (not including visibility). (200)

While this is a major assumption, there is other evidence that targeted policing operations do not affect illicit drug prices and purity in the short term. One study in Europe evaluated perceived and reported changes in price, purity and availability of heroin, cocaine and cannabis before and after a major police operation among users that were in and outside of the policing zone. Out of 174 users inside of the zone, over 80% reported no changes in price. When the investigators compared user responses inside of the zone and outside of the zone, there were no significant differences in perceived purity of heroin, cocaine or cannabis. (202)

Rosenblum et al. (2014) attempted to quantify and explain the relationship of heroin purity and price as it relates to race and ethnic differences in Philadelphia by neighborhood. While they did not explicitly evaluate policing in these racially segregated areas, they found that a certain type of heroin was associated with geographic areas where Puerto Rican individuals were clustered. Therefore, “oversampling” in this area would more than likely result in seized drugs that contain this type of heroin. (71) Unfortunately, we do not have a reference for making a valid estimate of what proportion of stamp bags we would expect to contain cocaine, fentanyl, or any other type of drug since historically stamp bags have been used for heroin.

To complicate matters more, there is mixed evidence on racial disparities in drug use and mortality patterns over the past few decades. While some studies have shown that cocaine-related mortality and drug use is more common among blacks (203-205), the evidence for this is weak and can be somewhat explained by other environmental, social and structural factors (206). The most recent mortality estimates from CDC indicate that while whites are more likely to die from an opioid-related overdose death, the rate of change of opioid-related mortality among blacks was larger between 2015 and 2016. (78)

8.4.1.3 Criminal Cases

These incidents, or drug seizures, are overly representative of criminal activity. Per the county evidence submission manual, drug evidence will not be tested if it is not linked to an open criminal case with charges. (149) We do not make sweeping conclusions about population drug use given this limitation, but rather indicate the population level of illicit drugs in the community.

8.4.1.4 Misclassification

The second possible source of bias could come from information bias during the manual sampling phase in the unit (circled on the right in the figure below). It is possible that there is systematic misclassification of stamp bags into the incorrect groups, but we assume that 1) if there is, it is not differential and 2) this is not the case and that the sorting procedure is a reliable method of classification.

The final source of misclassification bias could result during the address cleaning step during data cleaning. It seems unlikely, that there would be repeated misclassification of addresses to one jurisdiction over another given our two-step process. It is possible that there was systematic, differential misclassification of addresses to Pittsburgh zip codes, rather than the township or smaller municipalities. Some error may have resulted during Google searches of addresses, which typically remedied but still could result in incorrect coding. As a result, we would overestimate the significance of our clustering in the City of Pittsburgh.

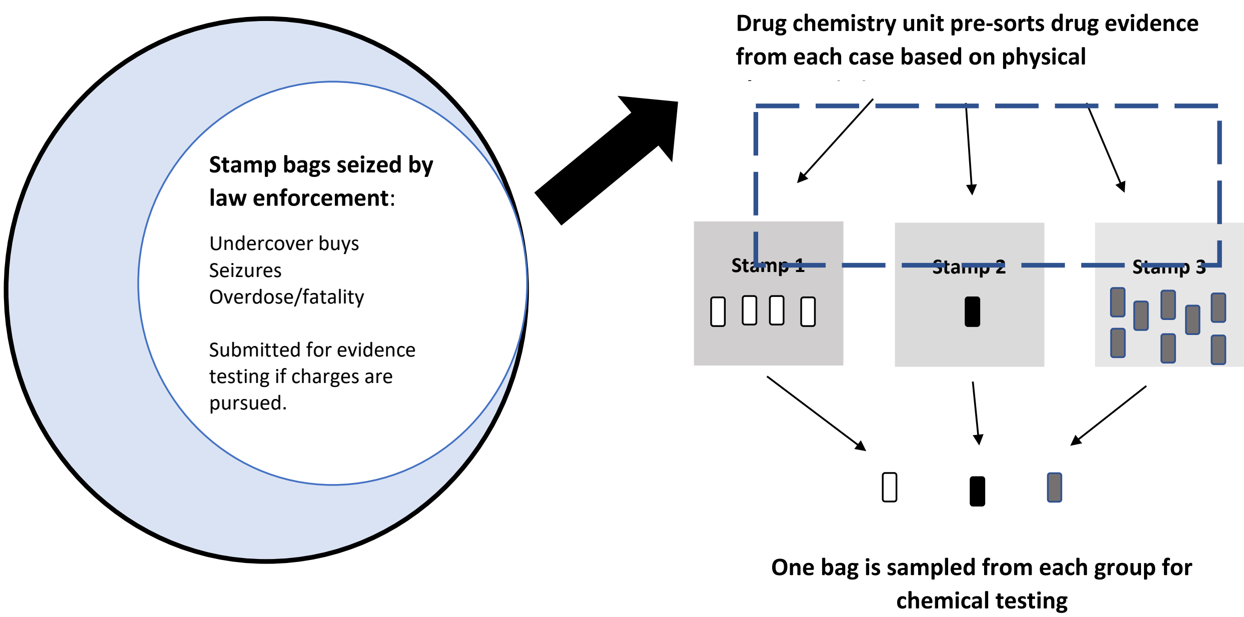

Figure 17: Schematic highlighted to show population of stamp bags that are not recovered by law enforcement, Allegheny County, PA

8.4.2 Study Design

Our study design is descriptive, and therefore we cannot draw conclusions about causality with respect to overdose mortality. However, these are some of the first public health analyses using this type of dataset; starting with descriptive epidemiology not only makes sense, but it is the correct first step in understanding the data and considering future study designs. In addition, the purpose of this dissertation was for practical use by the medical examiner office and drug chemistry unit rather than for making statistical comparisons among subgroups in the data.

8.4.3 Measurement

Measurement was challenging since there was no peer-reviewed literature on how to analyze or report stamp bag data, especially for hot spot analysis. However, we referenced surveillance reports, GIS experts and literature around drug-related activity to ensure that our drug categorization and reporting made sense with norms in public health and law enforcement.

We used counts, and not rates, for both thematic mapping and hot spot analysis. First and foremost, this limits comparisons for the burden of cases and/or bags across regions. As noted in Chapter 6.0, the comparisons across years for the same drug are difficult because the cut points change from year to year based on natural breaks in the data. While we could estimate the denominators for geographic regions using resident populations, we could not reasonably assume that the number of individuals associated with the incidents in that geographic region were actual residents of that region. It is well-established that drug activity crosses geographic borders, and both dealers and users will travel outside of their resident locality to purchase, sell, and use. (71, 196). As a result, we could not make valid comparisons about drug or risk differences between regions. However, we can still inform effective resource allocation to mitigate the effects of having elevated drug activity in distinct geographies.

The more difficult measurement issue was the replication of individual people both within and across years in the dataset. This was only pertinent in our calculation of demographic characteristics. We corrected for this using statistical de-duplication methods, but there is some degree of replication given we cannot determine differences for nicknames.

8.4.4 Generalizability

Not all counties in the United States have stamp bags on their streets. At first glance, it may seem that the results from these analyses are not generalizable to other jurisdictions with dissimilar types of drug evidence, and different partners or laboratories that test illicit drugs. However, these methods are adaptable for other public health or academic partnerships with law enforcement and can be used to describe any type of drug evidence (including counterfeit pills, patches, or unmarked bags). The uniqueness of the stamp bag is hardly a limitation, but an opportunity to explore illicit drug patterns in a time when illicit heroin and fentanyl are contributing to most of overdose deaths. Unlike unmarked bags, their unique markings are another possible data point that can be used to track different drug combinations in the community.

8.5 REVIEW OF STRENGTHS

These findings support the notion that while prescription opioid use, abuse and overdose continues to be a major public health problem, illicit opioids and other drugs are the biggest overdose threat in the county. Our findings are consistent with reports from the DEA and support other national entities that suggest Pennsylvania has a particularly high risk of heroin-related overdose deaths (119) especially in Southwestern Pennsylvania. (6) The upward trends in illicit fentanyl mirror those for fentanyl-related overdose deaths in Allegheny County, Pennsylvania (50), which suggests that our results are also consistent with local mortality trends and make sense in the context of what is occurring at the county level.

8.5.1.1 Timeliness

The most important and unique aspect of this dataset and the findings is the timeliness. Given the weekly processing and testing of drug evidence, we could access data from 2017 throughout the year as testing was completed. We were able to upload data for all incidents that occurred and were finalized for testing in 2017 on the first day of 2018. This was a critical part of our argument for using this data to enhance traditional surveillance since we could identify several new synthetic opioids that had not be previously detected in the county. We also could show drastic changes in fentanyl stamp bags from one year to the next, which was most obvious in 2017. These data demonstrate that there are alternative data around illicit opioids that is available to public health researchers and can be used to shed light on important aspects of the illicit side of the epidemic.

8.5.1.2 Gaps in Knowledge

Our initial literature searches revealed very little on the topic of distinct drug evidence types aside from standard law enforcement reports. The findings from this dissertation (particularly from the published results) help to fill a gap in knowledge around illicit drug patterns as they relate to public health. The methods offer a good starting point for future analyses and considerations where there are none in peer-reviewed literature; our published article was the first of its kind to appear in Medline for the search term “stamp bag.”

8.5.1.3 Sustainability

Using multiple statistical programs and data quality checks allowed for development of a technical instruction document that can be used for non-epidemiologists to work with the database. Though the raw datafiles will continue to be available and updated with additional data years, the local medical examiner office can still perform most of the analyses and construction steps using a program that they already have access to.

8.5.1.4 Inter-disciplinary Use

Construction of the database was a multi-disciplinary effort that involved law enforcement data, medical examiner and chemistry data, technical expertise, GIS expertise, and drug overdose expertise. Therefore, we aimed to create drug categorizations and deliverables that could be used by more than just public health researchers or epidemiologists.

8.5.1.5 Enhancement of Traditional Surveillance Methods

Currently, most illicit drug data that is used for public health surveillance comes from poison control centers (207), toxicology and death certificates, surveys (208) and law enforcement (145). More recently, EMS data has been used to demonstrate that it can function as a form of syndromic surveillance to detect or distinguish opioid-related overdoses where fentanyl, heroin or other illicit opioids may be involved. (209-211)

Poison control and EMS are unique in that they are timely and have not been used as standard forms of surveillance, but they can add additional information around the circumstances of the event and help account for limitations of current systems. (2011) They also demonstrate that our argument for using non-traditional data for public health purposes is plausible. Unlike these studies, we are not using a proxy measure for illicit drug activity but the actual drugs themselves. Our findings are consistently timely and are not limited to cases where there was a death (which broadens the relevance and scope of our results). We are not restricted by ICD-10 T coding (2012), which means we can detect and report characteristics of stamp bags that contain unusual or emerging illicit drugs. Additionally, if time and staffing allow we could theoretically identify illicit drugs that are circulating in stamp bags BEFORE anyone dies from it.

8.5.1.6 Linkage with other Datasets

One of the most relevant epidemiological strengths of this dataset and larger surveillance database is the ability to link other forms of data to it. Because the data in raw form contain identifiers, there is the possibility to link mortality, prescription medication, and other health data to the police records. Other non-health related data, such as census data, could also be linked to the geographic incident locations. If testing and time permitted, we could also add additional information about the stamp, diluents and adulterants to expand analyses around the bags.

Analyses using linked data would be particularly powerful, as they could establish various causal criteria for linking an overdose or overdose death with a stamp bag incident. While imperfect, it is another first step in establishing how these data can be incorporated into public health surveillance and research.

8.6 RECOMMENDATIONS, APPLICATIONS AND FUTURE USE

8.6.1 Recommendations

Based on the findings from this dissertation and the lessons learned in the process, we present several recommendations for data collection, management, cleaning, and sustainability:

1. Reach out to law enforcement and use findings to help improve data collection on scene, particularly for address information.
2. Consider requiring certain elements of address information at a minimum to improve future mapping
3. Collaborate with county statisticians or readily available university technical experts and students to automate a data upload and cleaning process for creating the database on local servers.
4. Re-visit and revise the process of geocoding addresses to increase the percentage that are matched to latitude and longitude. This process is timely and a limiting factor.
5. Develop a methodology for analyzing the stamps. With changes in data entry around the different types of drug evidence, it might be possible to estimate how many stamp bags are turned in for testing, how many bags are unstamped, and how the bags are different.

8.6.2 Applications and Uses

The surveillance database and the methods for this dissertation can be applied in several ways. First, the database can be maintained and use for future descriptive analyses, trend monitoring, time-varying analyses, and for querying cases. Second, the data (in limited form) could be made available as a public dataset to query or request data from for academic institutions, law enforcement, first responders, government, and other interested parties. Third, the methodologies and strategies from both the drug chemistry unit and this dissertation can be applied/adapted to other types of drug evidence and other laboratories across the county.

One way to use the database and findings is to provide timely reporting to stakeholders (e.g. law enforcement agencies) about their data quality metrics, local drug trends, and local threats. Developing an automated report from the system, automating the update process, and streamlining the data cleaning steps are also other ways to use the database and the data sources.
A second possible use is to develop methodology for analyzing the stamps themselves as markers of drug combinations, drug popularity, geographic patterns, and time trends. We did not analyze the stamps because of the large quantity each year and the variation among them, but they are the most unique aspect of this form of drug evidence and they are another opportunity for possible surveillance.

8.6.3 Conclusions

Far less is known about illicit drugs in the current opioid epidemic due to lack of accessible data around drugs like heroin. This dissertation adds new information about illicit opioids using drug evidence data at the local level, and our findings are consistent with current trends in mortality and other drug evidence reports. While the data are not collected for public health purposes, we demonstrate that they have a place in public health surveillance. Examining the types of illicit opioids that are found in the community as well as where they exist is important for on-the-ground prevention and response efforts, informing officials to help with decision-making, and generating new questions about the opioid epidemic.

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