CHILDREN IN THE UNITED STATES OPIOID EPIDEMIC

by

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ABSTRACT

This dissertation examines the needs of children growing up in families where a parent or caregiver is struggling with opioid-related problems. Because of their parents' illness, these children may be at increased risk for exposure to adverse or traumatic experiences. Indeed, a growing number of children are coming into contact with America's child welfare systems because of parents' opioid-related problems. These adverse childhood experiences may then increase children's risk for adult substance use disorder, creating a two-generational health problem. However, there are few research studies and even fewer policy initiatives focused on meeting the unique needs of these families.

This dissertation seeks to expand knowledge about children in the opioid epidemic with three aims:

- 1. Identify the number of families where an adult with an opioid use disorder lives with a child, and explore these adults' access to treatment (Chapter 2).
- Assess how childhood trauma influences the risk of heroin use at different ages in adults who have injected drugs (Chapters 3 & 4).
- Test if Florida's opioid prescribing reforms designed to prevent overdose deaths also helped reduce children's contact with the child welfare system (Chapters 5 & 6).

I address these aims using a combination of public surveys on drug use, administrative records on contact with the child welfare system, and primary data collection from adults who injected drugs in Baltimore. I show that:

1. Around 820,00 U.S. adults with an opioid use disorder live with at least one child, but fewer than a third report receiving any substance use treatment in the past year.

ii

- 2. Among adults who have injected drugs, a history of very high levels of childhood adversity is associated with elevated risk for sustained heroin use into late adulthood.
- 3. Florida's opioid prescribing reforms reduced drug overdose deaths, but did not have the added benefit of reducing children's contact with the child welfare system.

Findings suggest that existing strategies to address the opioid epidemic are not adequately meeting the unique needs of children, and specific, evidence-informed policies and programs are needed to address the unique needs of families struggling with opioid-related problems.

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iv

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v

TABLE OF CONTENTS

Title Page	i
Abstract	ii
Acknowledgments	iv
List of Tables	vii
List of Figures	ix
Chapter 1. Introduction	1
1.1. The United States Opioid Epidemic	2
1.2 The Pediatric Roots of Opioid-Related Problems	4
1.2.1 Childhood Adversity and Adult Health	4
1.2.2 Childhood Trauma and Opioids	5
1.3 Collateral Pediatric Consequences of the Opioid Epidemic	6
1.3.1 Opioid Use During Pregnancy	7
1.3.2 Maladaptive Parent-Child Interaction	7
1.3.3 Material Deprivation	9
1.3.4 Extended Separation	9
1.4 A Two-Generational Problem	10
1.5 Solutions and Barriers	11

1.5.1 Behavioral Health and Substance Use Treatment	11
1.5.2 Child Welfare	13
1.5.3 Courts	14
1.6 Summary and Motivation for Research	15
1.7 References	17
Chapter 2. U.S. Adults with Opioid Use Disorder Living with Children: Treatment Use and Barriers to Care	26
2.0 Abstract	27
2.1 Introduction	28
2.2 Materials and Methods	30
2.2.1 Study Population and Data	30
2.2.2. Measures	31
2.2.2.1 Exposure	32
2.2.2.2 Study outcomes	32
2.2.2.3 Demographics	33
2.2.3 Analytic Approach	33
2.3 Results	34
2.3.2 Treatment	34
2.3.3 Perceived Need for Treatment	35

2.4 Discussion	36
2.5 Conclusion	40
2.6 References	42
2.7 Exhibits	48
Chapter 3. Common Trajectories of Heroin and Cocaine Use Over the Life Course: A 30-Year Cohort Study of People Who Inject Drugs, 1988-2018	51
3.0 Abstract	52
3.1 Introduction	54
3.2 Materials and Methods	56
3.2.1 Study Participants	56
3.2.2 Measures	58
3.3.3 Analytic Approach	58
3.2.3.1 Single Class Model	59
3.2.3.2 Multiple Class Models	59
3.2.3.3. Sensitivity Analyses Participants Surviving to 2016	60
3.2.3.4 Inference	61
3.2.3.5 Software	61
3.3 Results	61
3.3.1 Sample Characteristics	61

3.3.2 Single-Class Model	61
3.3.2.1 Heroin	62
3.3.2.2 Cocaine	62
3.3.3 Model Selection	62
3.3.4 Best-Fitting Model	62
3.3.4.1 Heroin	62
3.3.4.2 Cocaine	63
3.3.5 Other Covariates	63
3.3.5.1 Heroin	63
3.3.5.2 Cocaine	64
3.3.6 Sensitivity Analyses Participants Surviving to 2016	64
3.4. Discussion	64
3.6 References	71
3.7 Exhibits	75
3.8 Appendix Exhibits	79
Chapter 4. Association of Childhood Adversity with Heroin and Cocaine Use Across the Adult Life Course of People Who Inject Drugs	83
4.0 Abstract	84
4.1 Introduction	85

4.2 M	aterials and Methods	87
4.2	2.1 Study Participants	87
4.2	2.2 Measures	89
	4.2.2.1 Outcome	89
	4.2.2.2 Exposure	89
	4.2.2.3 Effect Modifier	89
	4.2.2.4 Potential Confounders	90
4.2	2.3 Analytic Approach	91
	4.2.3.1 Summary	91
	4.2.3.2 Missing Questionnaire Responses	91
	4.2.3.3 Analytic Model	92
	4.2.4.4. Model Estimation	92
	4.2.4.5 Model Interpretation and Inference	93
	4.2.4.6 Software	94
4.3 Re	esults	94
4.	3.1 Demographics and Childhood Adversity	94
4.	3.2 Drug Use	94
	4.3.2.1 Heroin	94

4.3.2.2 Cocaine	94
4.3.3 Effect of Childhood Adversity	95
4.3.3.1 Heroin	95
4.3.3.2 Cocaine	95
4.4 Discussion	96
4.5 Conclusion	102
4.6 References	103
4.7 Exhibits	110
Chapter 5. Validating Bayesian Interrupted Time-Series Analysis to Study Florida's Opioid Prescribing Crackdown	114
5.0 Abstract	115
5.1 Introduction	116
5.1.1 Florida Reforms Targeting Opioid Prescribing	116
5.1.2 Secondary Effects of Florida Policy on Other Injury Deaths	117
5.1.3 Motivation and Hypotheses	118
5.2 Methods	119
5.2.1 Data	119
5.2.2 Study Sample	120
5.2.3 Analytic Approach	120

5.2.3.1 Brief Background on Bayesian Modeling.	121
5.2.3.2 Bayesian Structural Time Series Models (BSTS)	122
5.2.3.3 Model Fitting	123
5.2.3.4 Effect Estimation	123
5.2.3.5 Model Checking and Inference	124
5.2.3.6 Assumptions	125
5.2.3.7 Sensitivity Analysis – Poisoning Suicide	125
5.2.3.8 Software	125
5.3. Results	
5.3.1 Drug Overdose	125
5.3.2 Motor Vehicle Crash	126
5.3.3 Suicide	126
5.3.4 Model Checking	126
5.4. Discussion	127
5.4.1 Drug Overdose Deaths	127
5.4.2 Other Sources of Mortality	128
5.4.3 New Methods for Interrupted Time Series	129
5.4.4 Limitations	5.4.4

5.5 Conclusion	132
5.6 References	135
5.7 Exhibits	141
5.8 Appendix Exhibits	146
Chapter 6. Effect of Florida's Opioid Prescribing Crackdown on Child Welfare Involvement	151
6.0 Abstract	152
6.1 Introduction	153
6.1.1 The Opioid Epidemic and Child Welfare	153
6.1.2 Drug Policy and Child Welfare	154
6.1.3 Florida Reforms Targeting Opioid Prescribing	155
6.1.4 Secondary Effects of Florida Policy on Children and Families	155
6.2. Methods	156
6.2.1 Data	156
6.2.2 Study Sample	158
6.2.3 Measures	158
6.2.3.1 Physical Abuse Rate	159
6.2.3.2 Sexual Abuse Rate	159
6.2.3.3 Neglect Rate	159

6.2.3.4 Removal Rate	159
6.2.4 Analytic Approach	159
6.3 Results	161
6.4. Discussion	162
6.5 Conclusion	165
6.6. References	170
6.7 Exhibits	171
6.8 Appendix Exhibits	175
Chapter 7. Conclusion and Recommendations	179
7.1 Conclusion	180
7.1.1 Aim 1	180
7.1.1.1 Goal	180
7.1.1.2 Findings	180
7.1.1.3 Conclusion	181
7.1.2 Aim 2	181
7.1.2.1 Goal	181
7.1.2.2	181
7.1.2.3 Conclusions	182

7.1.3	182
7.1.3.1 Goal	182
7.1.3.2 Results	182
7.1.3.3 Conclusion	182
7.2 Recommendations	183
7.3 References	186
Bibliography	187
Curriculum Vitae	210

LIST OF TABLES

Table 2.1. Characteristics of U.S. Adults with Opioid Use Disorder, 2010-2014	48
Table 2.2. Association of Treatment Characteristics with Presence of Child in Household	49
Table 3.1. Prevalence of Drug Use, Characteristics, by Age Quartile at Visit	75
Table 3.2. Fit Statistics for Latent Class Models with 2-6 Classes	76
Table 3.1a. Prevalence of Drug Use, Characteristics, by Age Quartile at Visit, among Persons who Survived to 2016	79
Table 3.2a. Fit Statistics for Latent Class Models with 2-6 Classes, among Persons who Survived to 2016	80
Table 4.1. Adverse Childhood Experiences and Demographics of Baltimore City Adults who Have Injected Drugs	110
Table 4.2. Heroin and Cocaine Use and Characteristics of Baltimore City Adults who Have Injected Drugs, by History of Adverse Childhood Experiences	111
Table 4.3. Estimated Mean Predicted Probability and Relative Odds of Heroin and Cocaine Use by Age and History of Adverse Childhood Experiences	112
Table 5.1. Comparison States Included in Each Analysis	141
Table 5.2. Monthly Drug and Other Cause Mortality Rates and Counts Before and After Florida's Opioid Prescribing Crackdown Beginning July 2011	142
Table 5.3. Estimated Cumulative Percent Change in Mortality following Florida's Opioid Prescribing Crackdown, July 2011-July 2014	143

Table 6.1. Quarterly Counts and Rates of Child Welfare Contact Before and After Florida's Opioid Prescribing Crackdown Beginning July 2011	171
Table 6.2. Estimated Percent Change in Child Welfare Contact following Florida's Opioid Prescribing Crackdown, July 2011-July 2014	172

LIST OF FIGURES

Figure 2.1. Treatment Use and Perceived Need for Treatment by Presence of Child in Household, U.S. Adults with Opioid Use Disorder, 2010-2014	50
Figure 3.1. Single-Class (Pooled) and Six-Class Estimates of Predicted Probability of Heroin Use at Ages 30-60 in Baltimore Adults who Injected Drugs	77
Figure 3.2. Single-Class (Pooled) and Six-Class Estimates of Predicted Probability of Cocaine Use at Ages 30-60 in Baltimore Adults who Injected Drugs	78
Figure 3.1a. Single-Class (Pooled) and Six-Class Estimates of Predicted Probability of Heroin Use at Ages 30-60 in Baltimore Adults who Injected Drugs and Survived to 2017	81
Figure 3.2a. Single-Class (Pooled) and Six-Class Estimates of Predicted Probability of Cocaine Use at Ages 30-60 in Baltimore Adults who Injected Drugs and Survived to 2017	82
Figure 4.1 Estimated Predicted Probability of Heroin and Cocaine Use at Ages 30-65 by Exposure to Adverse Childhood Experiences in Baltimore Adults who Injected Drugs	83
Figure 5.1. Rates of Observed and Model-Estimated Mortality in Florida, 2005-2014.	144
Figure 5.2. Estimated Change in Mortality following Florida Opioid Prescribing Reform	145
Figure 5.1a. Estimated Effect of Florida Opioid Prescribing Crackdown on Drug Overdose Deaths: Florida vs Comparison States	146
Figure 5.2a. Estimated Effect of Florida Opioid Prescribing Crackdown on Motor Vehicle Crash Deaths: Florida vs Comparison States	147
Figure 5.3a. Estimated Effect of Florida Opioid Prescribing Crackdown on Suicide Deaths: Florida vs Comparison States	148
Figure 5.4a. Estimated Effect of Florida Opioid Prescribing Crackdown on Major Cardiovascular Disease Deaths: Florida vs Comparison States	149
Figure 5.5a. Estimated Effect of Florida Opioid Prescribing Crackdown on Malignant Neoplasm: Florida vs Comparison States	150
Figure 6.1. Rates of True and Model-Estimated Substantiated Maltreatment in Florida, 2003-2014.	173
Figure 6.2. Estimated Change in Child Maltreatment Incidents following Florida Opioid Prescribing Crackdown	174

Figure 6.1a. Estimated Effect of Florida Opioid Prescribing Crackdown on Substantiated Physical Abuse: Florida vs Control States	175
Figure 6.2a. Estimated Effect of Florida Opioid Prescribing Crackdown on Substantiated Sexual Abuse: Florida vs Control States	176
Figure 6.3a. Estimated Effect of Florida Opioid Prescribing Crackdown on Substantiated Neglect: Florida vs Control States	177
Figure 6.4a. Estimated Effect of Florida Opioid Prescribing Crackdown on Removals for Foster Care: Florida vs Control States	178

CHAPTER 1. INTRODUCTION

1.1. The United States' Opioid Epidemic

The United States is currently experiencing its worst-ever epidemic of drug related problems, an epidemic primarily attributable to opioids (National Institute on Drug Abuse, 2018).

Opioids are a class of drugs that act on the brain's opioid receptors to produce morphine-like effects (Hemmings & Egan, 2012). Opioids include morphine, prescription pain-relievers like Vicodin and OxyContin, illicit drugs like heroin, and powerful anesthetics like fentanyl. Some opioids are essential medications for pain management. However, improper use – for example, at very high doses or via rapid routes of administration that cause high concentrations of the drug to flood the brain – can lead to sensations of euphoria ("high") and, after repeated use, subsequent withdrawal. Both the high and withdrawal of opioid use can impair functioning and lead to craving for the drug. This makes opioids a class of drug with high potential for addiction (Kolodny et al., 2015).

Beginning in the early 1990s, pharmaceutical companies began to aggressively promote the idea that chronic pain was an untreated epidemic in the United States. Companies, in partnership with professional societies, advocated for more aggressive long-term management of chronic, non-cancer pain with opioid pain-relievers. Lowquality evidence was used to support the claim, now known to be inaccurate, that only a small subset of the population is at risk for opioid addiction, and that long-term use of these medications was safe for most people (Kolodny et al., 2015). In fact, there are still no randomized trials that demonstrate the effectiveness of opioid medications for long-

term management of chronic pain (Kolodny et al., 2015). Further, sustained opioid use rapidly produces physiological changes in the human brain (Younger et al., 2011).

Despite these concerns, over three decades, there was a dramatic increase in opioid pain-reliever prescriptions (Jones, 2013). This was accompanied by a nearly parallel increase in adverse health events caused by opioid use (Jones, 2013; Kolodny et al., 2015). Between 2001 and 2014, prescription opioid poisoning deaths increased threefold, to approximately 18,000 deaths per year. As noted, heroin is also an opioid drug, and it is likely many users who can no longer achieve high or access an opioid painreliever prescription transition to heroin. Indeed, in the period from 2002 to 2011, four out of five persons who initiated heroin use previously engaged in non-medical opioid pain-reliever use (Muhuri, Gfroerer, & Davies, 2013), and by 2014 heroin poisoning deaths had increased five-fold to 10,000 per year (National Institute on Drug Abuse, 2018). Since heroin is commonly injected, it can also increase risk for Hepatitis C and HIV. In recent years, extremely potent synthetic opioids like fentanyl have made their way into the heroin supply, often without users' knowledge, increasing users' risk of overdose and death (Miller, Stogner, Miller, & Blough, 2017; National Institute on Drug Abuse, 2018). The problem of opioid misuse has now become so severe that, in 2017, more than 2 million Americans were living with an opioid use disorder (Ahrnsbrak, Bose, Hedden, Lipari, & Park-Lee, 2017) and more than 72,000 people in the United States died from a drug overdose (National Institute on Drug Abuse, 2018). For the first time since the Centers for Disease Control (CDC) began collecting data on injury deaths, an American is more likely to die of poisoning than in a motor vehicle crash (National Center for Injury Prevention Control, 2016).

Most research on this opioid epidemic has focused on adults. This dissertation takes a different approach – it examines both the childhood risk factors that may contribute to the onset of opioid misuse, and the subsequent possible impact of a parent's opioid misuse on dependent children.

1.2. The Pediatric Roots of Opioid-Related Problems

Early-life risk factors that may influence the initiation and course of harmful opioid use have been a neglected area of research. Instead, most research on risk factors for opioid use disorder and overdose has focused on prescribing of opioid pain-relievers and diversion of opioid pain-relievers for non-medical use (Alexander, Frattaroli, & Gielen, 2015; Johnson et al., 2013; Kolodny et al., 2015; Muhuri et al., 2013). As the toll of illicit drugs like heroin and fentanyl has increased in recent years, there is also a growing research emphasis on expanding access to overdose prevention drugs like naloxone and medication-assisted addiction treatments (Alexander et al., 2015; Volkow, Frieden, Hyde, & Cha, 2014). This focus is consistent with a research agenda prioritizing proximal risk factors and treatment targets that can prevent overdose deaths and remedy an immediate overdose crisis. However, understanding the role of early-life risks of opioid-related problems is also important for two reasons: 1) Understanding how early life risks for opioid-related problems influence the *onset* of opioid misuse can help prevent the initiation of misuse by younger generations; 2) Understanding how early-life risks influence the *course* of opioid misuse can help improve the quality of treatment for the many Americans already suffering from an opioid use disorder.

1.2.1 Childhood Adversity and Adult Health

There are good reasons to believe that early life risk factors may influence the onset and course of opioid use disorder. There is strong evidence that exposure to maltreatment, household dysfunction, or other forms of adversity in childhood can increase risk for a wide range of mental, behavioral, and physical problems, including many of the leading causes of death (Anda et al., 2006; Felitti et al., 1998). Evidence from both observational studies in humans and randomized trials in animals show that trauma and deprivation in childhood lead to changes in adult brain regions and systems linked to addiction and psychopathology (Enoch, 2011). Exposure to childhood abuse or household dysfunction is a risk factor for substance use problems later in life (Dube et al., 2003), including use of "street drugs," earlier initiation of drug use and self-identified addiction to drugs. A history of child sexual abuse is associated with earlier initiation of injection drug use (Ompad et al., 2005). Children of adults with an alcohol use disorder are at elevated risk for alcohol use disorder, and there is some evidence this effect is partly mediated by children's exposure to adversity (Anda et al., 2006). This evidence suggests a history of trauma may be an important risk factor for opioid use disorder as well.

1.2.2 Childhood Trauma and Opioids

In fact, childhood trauma has been identified as a risk factor for an opioid use disorder specifically (Naqavi, Mohammadi, Salari, & Nakhaee, 2011). As compared to persons seeking treatment for nicotine or alcohol, persons seeking opioid treatment were more likely to have experienced a childhood trauma, and experienced trauma at an earlier age on average (Naqavi et al., 2011). One matched case control study found a history of child sexual abuse to be a risk factor for opioid use disorder among women, and a history

of physical and emotional abuse to be risk factors among men (Conroy, Degenhardt, Mattick, & Nelson, 2009). Indeed, some authors have argued that a history of childhood trauma plays a central role in the etiology of heroin use disorder (Darke, 2013).

Moreover, childhood adversity is a common antecedent for two other proximal risk factors for opioid-related problems. Specifically, childhood abuse and household dysfunction are associated with increased risk for both chronic pain (Davis, Luecken, & Zautra, 2005) and use of a greater number of prescription medications and medication classes (Anda, Brown, Felitti, Dube, & Giles, 2008).

Taken together, these findings suggest an important role for childhood adversity in the onset and course of opioid-related problems. A better understanding of this relationship may help improve prevention and treatment efforts.

1.3. Collateral Pediatric Consequences of the Opioid Epidemic

In addition to the *pediatric causes* of opioid-related problems, more research is needed to understand the *pediatric consequences* of the current opioid epidemic. While most public health responses to opioids target adult overdose (Alexander et al., 2015), with more than a million Americans over age 12 suffering from an opioid pain-reliever or heroin use disorder (Ahrnsbrak et al., 2017), the consequences of adult opioid use are likely spilling over and impacting children. In fact, in addition to increased adolescent use of opioid drugs (Ryan et al., 2016), there are at least four pathways by which increasing rates of opioid use by adults may be imposing collateral consequences on children and youth: 1) *maternal opioid use during pregnancy* and its teratogenic effects, 2) *maladaptive parent-child interaction* and insecure attachment resulting from the

effects of opioids on the brain, 3) *material deprivation* resulting from money and time spent on drugs, and 4) *extended separation from parents*.

1.3.1 Opioid Use During Pregnancy

While the teratogenic effects of opioids are less severe than those of alcohol and tobacco, opioid use during pregnancy can have harmful effects on the developing fetus (European Monitoring Center for Drugs and Drug Addiction, 2012). Specifically, opioid use during pregnancy is associated with low birth weight, premature birth, impaired intrauterine growth, and respiratory depression. If a fetus becomes physiologically dependent on opioids in the womb, it may experience the symptoms of opioid withdrawal including fever, excessive crying, irritability, and difficulty feeding; this is known as neonatal abstinence syndrome. If a mother injects opioids, this increases risk for bloodborne illness like HIV and Hepatitis C (HCV), which may be transmitted to the fetus. Further, opioid use during pregnancy has increased during the current opioid epidemic. Between 2000 and 2009, the rate of antepartum opioid use in the United States increased five-fold. Concomitantly, rates of neonatal abstinence syndrome increased three-fold (Patrick et al., 2012). This is probably the pediatric consequence of the opioid epidemic that has received the most attention from researchers (Patrick & Schiff, 2017).

1.3.2 Maladaptive Parent-Child Interaction.

Most drugs with high potential for substance use disorder act at least in part on the oxytocin and dopamine receptors that stimulate the reward and pleasure centers or the brain, and opioids are no exception (Renk et al., 2015). Importantly, there is evidence that these same pleasure-inducing systems play an important role in interpersonal bonding. In fact, evidence from animal models suggests that the impaired social bonding associated

with drug use is mediated by the action of these drugs on these pleasure centers in the brain (Renk et al., 2015; Young, Liu, Gobrogge, Wang, & Wang, 2014). This evidence suggests that opioid use may impair parents' ability to adaptively interact with their children, increasing their children's risk for insecure attachment (Renk et al., 2015), which is associated with long term negative effects on interpersonal interaction and adult psychopathology (Lyons-Ruth, Bureau, Easterbrooks, Obsuth, & Hennighausen, 2013; Mikulincer & Shaver, 2012).

Further, parent substance use generally is associated with decreased attentiveness to children's needs and more authoritarian parenting styles (Mayes et al., 1997; Wellisch & Steinberg, 1980). Both qualitative and quantitative studies of children with mothers in methadone maintenance have found that parents with opioid use disorder are disproportionately likely to engage in coercive parenting and high-risk behavior for child abuse perpetration (Barnard & McKeganey, 2004; Dawe & Harnett, 2007). Parent substance use is also associated with deficits in emotion regulation and parenting knowledge (Neger & Prinz, 2015). While these characteristics may not be caused by drug use, but instead may be a comorbid outcome of a history of life trauma (Patrick & Schiff, 2017), all of these behaviors found to be more prevalent in parents with substance use problems are risk factors for child abuse.

Finally, if parents are unable to adequately bond with, or supervise their children, this may increase risk for intentional or unintentional injury. Zip codes with higher rates of opioid overdoses also have higher rates of intentional and unintentional child injury, even after controlling for sociodemographic confounders (Wolf, Ponicki, Kepple, & Gaidus, 2016), and counties with higher rates of opioid-related problems also have higher

rates of substantiated child abuse (Ghertner, Baldwin, Crouse, Radel, & Waters, 2018). This is consistent with the shared epidemiology of child neglect and childhood injury (Peterson & Brown, 1994). It is also consistent with qualitative studies of parents in recovery from heroin use disorder, who describe behaviors that increase risk for unintentional injury – such as failing to supervise children – and intentional injury – such as failing to protect children from abuse by intimate partners (McKeganey, Barnard, & McIntosh, 2002).

1.3.3 Material Deprivation.

Substance use disorders are extremely costly to the user. Qualitative studies of mothers in treatment for heroin use paint a picture of parents strapped for the time and money needed to adequately care for children. In one qualitative study, parents in recovery from heroin use disorder reported that, during the time when they were using, they spent money on drugs instead of on food or clothing for children, failed to establish regular household routines, and experienced extended periods of separation from their children (McKeganey et al., 2002). Quantitative findings are similarly bleak. One study of 100 daily, untreated heroin users in Detroit found that participants spent an extraordinary 72 percent of their income on heroin and another 11 percent on cigarettes and alcohol, with only 12 percent dedicated to food and shelter (Roddy & Greenwald, 2009). All of this suggests that many children of parents with an opioid use disorder may suffer from the adverse effects of growing up in poverty.

1.3.4 Extended Separation

Finally, a parent's opioid use disorder can lead to extended periods of parent child separation. An early study of mothers participating in methadone treatment found that 80

percent were arrested at least once during the time the child was growing up and 14 percent were hospitalized for an emotional disorder (Kolar, Brown, Haertzen, & Michaelson, 1994), experiences that could lead to extended periods of separation between parent and child. Further, if parents struggling with opioid use disorder are unable to adequately care for their children, this can lead to children being placed in foster care. While precise estimates vary, studies have consistently found a high prevalence of substance use problems among families involved with the child welfare system (Barth, 2009; Traube, 2012), particularly among infants (Wulczyn, Ernst, & Fisher, 2011). More recent research has specifically linked escalating rates of opioid-related problems to increases in the number of children entering foster care (Ghertner et al., 2018), and child welfare agencies across the country report that there are children entering and remaining into foster care for extended periods of time because of parent opioid use problems (Radel, Baldwin, Crouse, Ghertner, & Waters, 2018).

1.4 A Two-Generational Problem

In summary, the research presented suggests that the opioid epidemic poses numerous threats to children, and that existing prevention, child protection, social insurance, and treatment services are not adequate to address these threats. Thus, the epidemic is likely increasing the number of children exposed to "polyvictimization" and "complex trauma" (Finkelhor, Ormrod, Turner, & Hamby, 2005) – exposure to a large number of diverse, chronic, adverse experiences spread over the course of childhood. As already discussed, these experiences are associated with increased long term risk for a wide range of antisocial behaviors, unhealthy behaviors, mental disorders, chronic diseases, and suicide (Finkelhor et al., 2005), along with, most pertinently, the onset of

opioid use disorder. Thus, if the pediatric implications of the current opioid epidemic remain under-addressed, long-term behavioral health consequences are likely to persist even if efforts to prevent adult overdose are successful. In this way, the current opioid epidemic lays the groundwork for a future epidemic of opioid-related or other health problems.

1.5. Solutions and Barriers

Adequately meeting the needs of families struggling with opioid-related problems and interrupting the intergenerational health threats described above requires collaboration between three systems – behavioral health and substance use treatment systems, child welfare systems, and the courts (Feder, Letourneau, & Brook, 2018). Unfortunately, collaboration between these systems is often poor and misinformation about best practices in one system will abound in the others (Feder et al., 2018; Stedt & DeCerchio, 2016).

1.5.1 Behavioral Health and Substance Use Treatment.

Behavioral health systems are responsible for providing parents and pregnant women with opioid-related problems with the evidence-based treatments they need to avoid overdose, regain agency over their lives, and adequately care for their children.

The best supported treatments for opioid use disorder are "medication-assisted" – they supplement traditional counseling and behavioral therapies with medications like methadone and buprenorphine to ameliorate the neurologic changes induced by extended opioid use. These medications prevents the agonizing symptoms of opioid withdrawal, reduce the risk of relapse to illicit use, and improve functioning (Connery, 2015; Volkow et al., 2014).

The benefits of medication-assisted treatment have been specifically studied and demonstrated in pregnant women (Wong et al., 2011), for whom medication maintenance increases participation in prenatal care, reduces risk of harm to the mother and fetus, and is clearly preferred to detoxification without medication in nearly all cases (Heberlein, Leggio, Stichtenoth, & Thomas, 2012; Patrick & Schiff, 2017). Further, new research offers evidence that when parents involved with the child welfare system receive medication-assisted treatment, they are reunified with their children more rapidly (Hall, Wilfong, Huebner, Posze, & Willauer, 2016; Radel, Baldwin, Crouse, Ghertner, & Waters, 2018a).

It is also essential to have a holistic approach to care prepared to meet the challenging psychosocial comorbidities that often accompany opioid use, and, in the case of pregnant women, to treat neonatal abstinence symptoms after birth (Winklbaur et al., 2008). Women are more likely to remain in treatment if childcare is provided onsite, and if providers engage in trauma-informed practice (Patrick & Schiff, 2017).

In summary, medication-assisted treatment supplemented by specialty services for parents and pregnant women are a cornerstone of meeting the needs of children growing in families struggling with opioid-related problem.

Unfortunately, medication-assisted treatment for opioid use disorder is both unavailable and underused in the general population, with a likely a gap of nearly one million people nationally who could benefit from methadone or buprenorphine treatment but do not receive any (Jones, 2013). There are likely particularly severe access problems for pregnant women and child welfare involved parents (Patrick & Schiff, 2017; Radel et al., 2018a). Only 19 states have even a single substance use treatment program

specializing in pregnant women, and only 15 percent of substance use treatment centers offer specialty services for pregnant women. There is a particular shortage of treatment for pregnant women in rural areas (Patrick & Schiff, 2017; Radel et al., 2018a), where illicit opioid use has increased fastest. Further, as discussed below, misconceptions regarding and stigma toward medication-assisted treatment may deter parents from receiving appropriate care (Radel et al., 2018a).

1.5.2 Child Welfare

Child welfare services provide an important complement to treatment for parents, ensuring the unique needs of children are met while their parents receive treatment, as well as facilitating access to or providing other services to help the family unit heal. First among those other services is substance use treatment, and child welfare agencies can and should facilitate access to medication-assisted treatment for parents (Radel et al., 2018a).

However, child welfare agencies also play an important role in providing parenting and family support services. There are a number of parenting interventions that either explicitly target or have been adapted to parents with substance use disorders (Neger & Prinz, 2015). One review of programs appearing in scientific literature found that programs tend to be effective when the parenting intervention is started immediately alongside initiation of substance use treatment, when significant others are included as key partners in treatment, and when transportation and lack of childcare are not barriers to treatment (Neger & Prinz, 2015). Most evidence-based programs rely on some combination of cognitive-behaviorally informed parenting intervention, relapse prevention techniques to address substance use, and efforts to facilitate access to needed

social and medical services (Grant, Ernst, Streissguth, & Stark, 2005; Haggerty, Skinner, Fleming, Gainey, & Catalano, 2008; Renk et al., 2015).

Unfortunately, substance use treatment and child welfare fields remain balkanized (Staton-Tindall, Sprang, Clark, Walker, & Craig, 2013). Just as substance use treatment programs may not be adequately equipped to accommodate the special needs of parents and pregnant women, child welfare agencies are often ill-informed about best practices for treating substance use disorders. In particular, misperceptions of medication-assisted treatment abound among child welfare workers, which may prevent parents from being referred to program that offer the most effective care (Radel et al., 2018a). Additionally, child welfare agencies may operate on constricted legally-imposed timelines requiring reunification or termination of parental rights by particular deadlines; these timelines may not be consistent with the normal course of opioid use disorder treatment, which can take many years, can be characterized by periods of relapse and remission, and often involves indefinite maintenance on medication.

1.5.3 Courts

Finally, courts have enormous decision-making authority for both adults who use substances illicitly and adults involved with the child welfare system. Informed legal decision making and well-structured court programs can facilitate access to substance use treatment programs, expedite the child welfare process, and help overcome the systemic divide between behavioral health and child welfare described above. This has been demonstrated by family drug courts – specialized dockets that divert drug-using parents into treatment – that have been shown to increase treatment retention and reduce foster care time (Marlowe & Carey, 2012; Stedt & DeCerchio, 2016). Conversely, when courts

are ill-informed, they may order decisions that are not in the best interest of the child, such as requiring parents to terminate medication-assisted treatment, or terminating parental rights solely because of an episode of relapse into illicit use.

1.6 Summary and Motivation for Research

In summary:

- 1. A growing number of children are likely at risk for adversity, trauma, and child welfare involvement as a result of the opioid epidemic.
- 2. This exposure to adversity and trauma resulting from parent substance use may in turn increase these children's risk for adult health problems, including opioid misuse, creating a two-generational health burden.
- 3. There are policies and services that may help families heal from or avert these health harms, but poor coordination between substance use, child welfare, and justice systems may impede parents access to these services.

If these challenges are not addressed, increases in the prevalence of childhood adversity resulting from the opioid epidemic could transform a short-term public health crisis into a long-term burden on population health.

The remainder of this dissertation examines a number of important questions about children in the opioid epidemic. **Aim 1** (Chapter 2) makes the first estimate of the number of households with children where an adult has an opioid use disorder. It then examines the prevalence of substance use treatment utilization among the adults in these household. Finally, it examines if these adults living with children face unique barriers to care that are less common among their counterparts without children. **Aim 2** examines how childhood adversity can influence the course of adult opioid misuse. A pre-analysis

(Chapter 3) explores heterogeneity in common trajectories of heroin use over the life course. Then, in the main analysis (Chapter 4), self-reported childhood adversity is examined as a predictor of a more severe trajectory of substance use. Finally, **Aim 3** examines one important policy effort designed to combat the opioid epidemic – Florida's initiative to reduce irresponsible opioid prescribing through the introduction of a Prescription Drug Monitoring Program (PDMP) and a crackdown on negligent independent pain management clinics ("pill mills"). In a pre-analysis, (Chapter 5) a new method – Bayesian structural time series (BSTS) – is presented for evaluating the impact of new state policies. Then, BSTS is validated for the present study by replicating a published positive finding that the aforementioned prescribing reforms prevented overdose deaths. Finally (Chapter 6), BSTS is used again to determine if Florida's intervention had the ancillary benefit of preventing contact with the child welfare system.

Collectively, these research projects provide important new information that can help policy makers 1) address the needs of adults with opioid use disorder who have a history of childhood trauma, and 2) prevent the transmission of that trauma to a future generation of children through evidence-informed services and policies that meet the needs of families struggling with opioid-related problems.

1.7 References

- Ahrnsbrak, R., Bose, J., Hedden, S. L., Lipari, R. N., & Park-Lee, E. (2017). Key substance use and mental health indicators in the United States: Results from the 2016 National Survey on Drug Use and Health. *Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration: Rockville, MD, USA.*
- Alexander, G. C., Frattaroli, S., & Gielen, A. C. (2015). *The Prescription Opioid Epidemic: An Evidence-Based Approach*. Johns Hopkins Bloomberg School of Public Health,© 2015.
- Anda, R. F., Brown, D. W., Felitti, V. J., Dube, S. R., & Giles, W. H. (2008). Adverse childhood experiences and prescription drug use in a cohort study of adult HMO patients. *BMC Public Health*, 8(1), 198.
- Anda, R. F., Felitti, V. J., Bremner, J. D., Walker, J. D., Whitfield, C. H., Perry, B. D., ... Giles, W. H. (2006). The enduring effects of abuse and related adverse experiences in childhood. *European Archives of Psychiatry and Clinical Neuroscience*, 256(3), 174–186.
- Barnard, M., & McKeganey, N. (2004). The impact of parental problem drug use on children: what is the problem and what can be done to help? *Addiction*, 99(5), 552–559.
- Barth, R. P. (2009). Preventing child abuse and neglect with parent training: Evidence and opportunities. *The Future of Children*, *19*(2), 95–118.
- Connery, H. S. (2015). Medication-assisted treatment of opioid use disorder: review of the evidence and future directions. *Harvard Review of Psychiatry*, *23*(2), 63–75.

- Conroy, E., Degenhardt, L., Mattick, R. P., & Nelson, E. C. (2009). Child maltreatment as a risk factor for opioid dependence: Comparison of family characteristics and type and severity of child maltreatment with a matched control group. *Child Abuse & Neglect*, 33(6), 343–352.
- Darke, S. (2013). Pathways to heroin dependence: time to re-appraise self-medication. *Addiction*, *108*(4), 659–667.
- Davis, D. A., Luecken, L. J., & Zautra, A. J. (2005). Are reports of childhood abuse related to the experience of chronic pain in adulthood?: a meta-analytic review of the literature. *The Clinical Journal of Pain*, 21(5), 398–405.
- Dawe, S., & Harnett, P. (2007). Reducing potential for child abuse among methadonemaintained parents: Results from a randomized controlled trial. *Journal of Substance Abuse Treatment*, 32(4), 381–390.
- Dube, S. R., Felitti, V. J., Dong, M., Chapman, D. P., Giles, W. H., & Anda, R. F. (2003).
 Childhood abuse, neglect, and household dysfunction and the risk of illicit drug use: the adverse childhood experiences study. *Pediatrics*, *111*(3), 564–572.
- Enoch, M.-A. (2011). The role of early life stress as a predictor for alcohol and drug dependence. *Psychopharmacology*, *214*(1), 17–31.

European Monitoring Center for Drugs and Drug Addiction. (2012). *Pregnancy, Childcare and the Family: Key Issues for Europe's Response to Drugs*. Retrieved from Publications Office of the European Union website: http://www.emcdda.europa.eu/system/files/publications/671/TDSI12001ENC_39 6469.PDF

- Feder, K. A., Letourneau, E. J., & Brook, J. (2018). Children in the Opioid Epidemic: Addressing the Next Generation's Public Health Crisis. *Pediatrics*, e20181656. https://doi.org/10.1542/peds.2018-1656
- Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V.,
 ... Marks, J. S. (1998). Relationship of childhood abuse and household
 dysfunction to many of the leading causes of death in adults: The Adverse
 Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine*,
 14(4), 245–258.
- Finkelhor, D., Ormrod, R., Turner, H., & Hamby, S. L. (2005). The victimization of children and youth: a comprehensive, national survey. *Child Maltreatment*, 10(1), 5–25. https://doi.org/10.1177/1077559504271287
- Ghertner, R., Baldwin, M., Crouse, G., Radel, L., & Waters, A. (2018). The relationship between substance use indicators and child welfare caseloads. *ASPE*. Retrieved from

https://aspe.hhs.gov/system/files/pdf/258831/SubstanceUseCWCaseloads.pdf

- Grant, T. M., Ernst, C. C., Streissguth, A., & Stark, K. (2005). Preventing alcohol and drug exposed births in Washington State: Intervention findings from three Parent-Child Assistance Program sites. *The American Journal of Drug and Alcohol Abuse*, 31(3), 471–490.
- Haggerty, K. P., Skinner, M., Fleming, C. B., Gainey, R. R., & Catalano, R. F. (2008).Long-term effects of the Focus on Families project on substance use disorders among children of parents in methadone treatment. *Addiction*, *103*(12).

- Hall, M. T., Wilfong, J., Huebner, R. A., Posze, L., & Willauer, T. (2016). Medication-Assisted Treatment Improves Child Permanency Outcomes for Opioid-Using Families in the Child Welfare System. *Journal of Substance Abuse Treatment*, *71*, 63–67.
- Heberlein, A., Leggio, L., Stichtenoth, D., & Thomas, H. (2012). The treatment of alcohol and opioid dependence in pregnant women. *Current Opinion in Psychiatry*, 25(6), 559.
- Hemmings, H. C., & Egan, T. D. (2012). Pharmacology and physiology for anesthesia: foundations and clinical application. Elsevier Health Sciences.
- Johnson, E. M., Lanier, W. A., Merrill, R. M., Crook, J., Porucznik, C. A., Rolfs, R. T., & Sauer, B. (2013). Unintentional prescription opioid-related overdose deaths: description of decedents by next of kin or best contact, Utah, 2008–2009. *Journal* of General Internal Medicine, 28(4), 522–529.
- Jones, C. M. (2013). Trends in the distribution of selected opioids by state, US, 1999– 2011. *National Meeting Safe State Alliance*.
- Kolodny, A., Courtwright, D. T., Hwang, C. S., Kreiner, P., Eadie, J. L., Clark, T. W., & Alexander, G. C. (2015). The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. *Annual Review of Public Health*, *36*, 559–574.
- Lyons-Ruth, K., Bureau, J.-F., Easterbrooks, M. A., Obsuth, I., & Hennighausen, K. (2013). Parsing the Construct of Maternal Insensitivity: Distinct Longitudinal Pathways Associated with Early Maternal Withdrawal. *Attachment & Human Development*, 15(0). https://doi.org/10.1080/14616734.2013.841051

- Marlowe, D., & Carey, S. (2012). Research update on family drug courts. Retrieved from http://www.nadcp.org/wpcontent/uploads/Reseach%20Update%20on%20Family%20Drug%20Courts%20-%20NADCP.pdf
- Mayes, L. C., Feldman, R., Granger, R. H., Haynes, O. M., Bornstein, M. H., & Schottenfeld, R. (1997). The effects of polydrug use with and without cocaine on mother-infant interaction at 3 and 6 months. *Infant Behavior and Development*, 20(4), 489–502.
- McKeganey, N., Barnard, M., & McIntosh, J. (2002). Paying the price for their parents' addiction: meeting the needs of the children of drug-using parents. *Drugs: Education, Prevention and Policy*, 9(3), 233–246.
- Mikulincer, M., & Shaver, P. R. (2012). An attachment perspective on psychopathology. *World Psychiatry*, 11(1), 11–15.
- Miller, J. M., Stogner, J. M., Miller, B. L., & Blough, S. (2017). Exploring synthetic heroin: Accounts of acetyl fentanyl use from a sample of dually diagnosed drug offenders. *Drug and Alcohol Review*.
- Muhuri, P. K., Gfroerer, J. C., & Davies, M. C. (2013). Associations of nonmedical pain reliever use and initiation of heroin use in the United States. *CBHSQ Data Review*, 17.
- Naqavi, M. R., Mohammadi, M., Salari, V., & Nakhaee, N. (2011). The relationship between childhood maltreatment and opiate dependency in adolescence and middle age. *Addiction & Health*, *3*(3–4), 92.

National Center for Injury Prevention Control. (2016). 10 Leading Causes of Injury Deaths by Age Group Highlighting Unintentional Injury Deaths, United States – 2014 (Vol. 2017). Retrieved from

https://www.cdc.gov/injury/wisqars/pdf/leading_causes_of_injury_deaths_highlig hting_unintentional_injury_2014-a.pdf

- National Institute on Drug Abuse. (2018, August 9). Overdose Death Rates. Retrieved December 6, 2018, from https://www.drugabuse.gov/related-topics/trendsstatistics/overdose-death-rates
- Neger, E. N., & Prinz, R. J. (2015). Interventions to address parenting and parental substance abuse: Conceptual and methodological considerations. *Clinical Psychology Review*, 39, 71–82.
- Ompad, D. C., Ikeda, R. M., Shah, N., Fuller, C. M., Bailey, S., Morse, E., ... Vlahov, D. (2005). Childhood sexual abuse and age at initiation of injection drug use. *American Journal of Public Health*, 95(4), 703–709.
- Patrick, S. W., & Schiff, D. M. (2017). A Public Health Response to Opioid Use in Pregnancy. *Pediatrics*, e20164070.
- Patrick, S. W., Schumacher, R. E., Benneyworth, B. D., Krans, E. E., McAllister, J. M.,
 & Davis, M. M. (2012). Neonatal abstinence syndrome and associated health care expenditures: United States, 2000-2009. *Jama*, 307(18), 1934–1940.
- Peterson, L., & Brown, D. (1994). Integrating child injury and abuse-neglect research: common histories, etiologies, and solutions. *Psychological Bulletin*, *116*(2), 293.
- Radel, L., Baldwin, M., Crouse, G., Ghertner, R., & Waters, A. (2018a). *Medication-Assisted Treatment for Opioid Use Disorder in the Child Welfare Context:*

Challenges and Opportunities. Retrieved from ASPE website: https://aspe.hhs.gov/pdf-report/medication-assisted-treatment-opioid-usedisorder-child-welfare-context-challenges-and-opportunities

Radel, L., Baldwin, M., Crouse, G., Ghertner, R., & Waters, A. (2018b). Substance use, the opioid epidemic, and the child welfare system: Key Findings from a Mixed Methods Study. *ASPE*. Retrieved from https://aspe.hhs.gov/system/files/pdf/258836/SubstanceUseChildWelfareOvervie w.pdf

- Renk, K., Boris, N. W., Kolomeyer, E., Lowell, A., Puff, J., Cunningham, A., ...
 McSwiggan, M. (2015). The state of evidence-based parenting interventions for parents who are substance-involved. *Pediatric Research*, 79(1–2), 177–183.
- Roddy, J., & Greenwald, M. (2009). An economic analysis of income and expenditures by heroin-using research volunteers. *Substance Use & Misuse*, 44(11), 1503–1518.
- Ryan, S. A., Gonzalez, P. K., Patrick, S. W., Quigley, J., Siqueira, L., & Walker, L. R. (2016). Medication-assisted treatment of adolescents with opioid use disorders. *Pediatrics*, 138(3), e20161893.
- Stedt, E. V., & DeCerchio, K. (2016, August). Regional Partnership Grants Collaborative Approaches: Lessons Learned from the RPG Program. Presented at the Child Welfare League of America National Conference, Orange County, California, USA. Retrieved from https://www.cwla.org/wpcontent/uploads/2016/09/D3_Workshop_RPG_Final.pdf

- Traube, D. E. (2012). The Missing Link to Child Safety, Permanency, and Well-Being:
 Addressing Substance Misuse in Child Welfare. *Social Work Research*, *36*(2),
 83–87. https://doi.org/10.1093/swr/svs043
- Volkow, N. D., Frieden, T. R., Hyde, P. S., & Cha, S. S. (2014). Medication-assisted therapies—tackling the opioid-overdose epidemic. *New England Journal of Medicine*, 370(22), 2063–2066.
- Wellisch, D. K., & Steinberg, M. R. (1980). Parenting attitudes of addict mothers. International Journal of the Addictions, 15(6), 809–819.
- Wolf, J. P., Ponicki, W. R., Kepple, N. J., & Gaidus, A. (2016). Are community level prescription opioid overdoses associated with child harm? A spatial analysis of California zip codes, 2001–2011. Drug and Alcohol Dependence, 166, 202–208.
- Wong, S., Ordean, A., Kahan, M., Gagnon, R., Hudon, L., Basso, M., ... Delisle, M.-F. (2011). Substance use in pregnancy. *Journal of Obstetrics and Gynaecology Canada*, 33(4), 367–384.
- Wulczyn, F., Ernst, M., & Fisher, P. (2011). Who are the Infants in Out-of-home Care?: An Epidemiological and Developmental Snapshot. Chapin Hall.
- Young, K. A., Liu, Y., Gobrogge, K. L., Wang, H., & Wang, Z. (2014). Oxytocin reverses amphetamine-induced deficits in social bonding: evidence for an interaction with nucleus accumbens dopamine. *Journal of Neuroscience*, 34(25), 8499–8506.
- Younger, J. W., Chu, L. F., D'Arcy, N. T., Trott, K. E., Jastrzab, L. E., & Mackey, S. C. (2011). Prescription opioid analgesics rapidly change the human brain. *PAIN®*, *152*(8), 1803–1810.

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CHAPTER 2. U.S. ADULTS WITH OPIOID USE DISORDER LIVING WITH CHILDREN: TREATMENT USE AND BARRIERS TO CARE

2.0 Abstract

Background: U.S. adults with an opioid use disorder who live with a child have unique treatment needs, but little is known about the treatment use of these adults.

Methods: Data come from the 2010-2014 versions of the National Survey on Drug Use and Health, an annual survey assessing substance use in the United States. Adults (>=18) with a heroin or pain-reliever use disorder living in a household with a child (<18) were compared to adults not living with children on their use of substance use treatment, treatment settings, payment sources, perceived unmet need for treatment, and barriers to care using logistic regression to adjust for demographic differences between groups.

Results: Of the approximately 820,000 adults with an opioid use disorder living with at least one child, 28% reported receiving any past-year substance use treatment, a rate comparable to adults not living with a child (30%). Among adults reporting unmet treatment need, those who lived with a child were more likely to report that access barriers like not being able to find the right kind of program (aOR 2.9, 95% CI 1.2 – 7.1), as well as stigma (aOR 4.1, 95% CI 1.5 to 11.2), kept them from receiving care.

Conclusion: The majority of adults with OUD do not receive care. Adults with OUD who reside with children may face unique barriers to accessing treatment.

2.1 Introduction

The United States is currently experiencing its worst ever epidemic of drugrelated problems, an epidemic driven primarily by opioids. With at least 2 million Americans suffering from an opioid use disorder, as discussed in the introductory chapter, there is growing evidence that this epidemic of adult opioid use is spilling over and increasing the risk that children will be exposed to toxic stress, trauma and other negative consequences as a result of parental use. Research shows that experiences of trauma and deprivation in childhood are robust risk factors for a host of chronic health conditions across the life course (Anda et al., 2006; Felitti et al., 1998; Lamont, 2010), including adult substance use problems (Dube et al., 2003). Without an adequate public response to meet the needs of these children and their families, there is a risk that today's acute opioid crisis will evolve into a longer term, chronic health burden for the next generation related to increased likelihood of adverse exposures described in the Introduction.

An essential strategy for meeting the needs of children affected by the opioid epidemic is ensuring their parents and caregivers have access to evidence-based treatment. Among families involved in the child welfare system, facilitating parents' access to medication-assisted treatment for opioid use improves the safety and developmental appropriateness of parent-child interactions, and is associated with increased odds of parent-child reunification following a foster care placement (Hall, Wilfong, Huebner, Posze, & Willauer, 2016).

Unfortunately, fewer than one-third of Americans with opioid use disorder receive any treatment, and fewer than a third of those in treatment receive medication-

assisted treatment (Feder et al., 2017; Krawczyk, Feder, Fingerhood, & Saloner, 2017). A number of factors may contribute to this need-treatment gap including a lack of perceived need for treatment (Ali, Teich, & Mutter, 2015), inability to pay for treatment (Feder et al., 2017), a shortage of providers (Jones, Campopiano, Baldwin, & McCance-Katz, 2015), and stigma associated with seeking care.

There are reasons to believe that the treatment patterns and barriers faced by parents with dependent children are different from those of childless adults or adults whose children are grown or no longer in their care. In his classic healthcare utilization model, Andersen describes three sets of factors that can influence utilization of healthcare: 1) predisposing characteristics such as demographics, 2) real or perceived need for care, and 3) enabling resources or barriers to care (Andersen, 1995). Parents and caregivers with opioid use disorders may differ from their counterparts without dependent children on all three of these factors: 1) Parents and caregivers may be demographically different from adults without dependent children; 2) The desire to be a good parent or "be there" for children may influence perceived need for treatment, and has been reported in qualitative studies as a reason parents choose to seek care (Barnard & McKeganey, 2004). 3) Parents and caregivers may face unique barriers to care – for example, a shortage of family-friendly treatment programs or a lack of childcare; and parents and caregivers may also have unique enabling factors - for example, increased likelihood of Medicaid eligibility due to higher income eligibility limits for parents in some states. Understanding the current service access and utilization of adults with opioid use disorder who have children – and how these adults differ from adults without

dependent children – can inform a public health response to the opioid epidemic that addresses the epidemic's effects on children and families.

This paper uses data from a nationally representative survey to describe the substance use treatment access and utilization of adults who have an opioid use disorder and are living with children under age 18, and compare these adults living with children to their counterparts not living with children under age 18. It seeks to answer the following questions:

- What proportion of adults living with children have an opioid use disorder?
 What are the demographic characteristics of this population?
- 2. What proportion of adults with an opioid use disorder who live with children receive substance use treatment? In what settings do they receive treatment and who pays for their care?
- **3.** What proportion of adults with an opioid use disorder who live with children perceive a need for substance use treatment? What barriers do these adults face in receiving care?

In all cases, these characteristics are compared to adults with opioid use disorder who are not living with children, to better understand the unique treatment landscape facing adults with an opioid use disorder who live with children.

2.2 Materials and Methods

2.2.1. Study Population and Data

The National Survey on Drug Use and Health (NSDUH) is an annual, nationally representative survey of the U.S. households conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA). Respondents are asked about their use of alcohol, tobacco, and other drugs; about the use of substance use treatment; and about an array of experiences and conditions thought to be related to substance use, including substance use disorders, mental health problems, and physical health problems. Data for this study are drawn from the 2010-2014 NSDUHs. Beginning in 2015, the NSDUH prescription drug module was revised to begin identifying people who used prescription drugs as directed by a doctor; this broadened the pool of respondents assessed for a pain-reliever use disorder. For this reason, 2010-2014 was selected as the most recent consecutive five-year period in which survey questions were comparable across the full period (Quast, Storch, & Yampolskaya, 2018; Wolf, Ponicki, Kepple, & Gaidus, 2016). SAMHSA provides a cleaned and anonymized version of the dataset online for public use through its Substance Abuse and Mental Health Data Archive (SAMHDA) (SAMHSA, n.d.).

The study population was comprised of adults (18 or older) who met criteria for an opioid use disorder in the year preceding their interview. This included participants who reported using a pain-reliever in a manner other than prescribed by a doctor, as well participants who reported heroin use. Use disorder was defined as meeting criteria for DSM-IV substance abuse or dependence. Because all variables used in the analysis were statistically imputed by SAMHSA prior to making data publicly available, there are no missing observations. The final population consisted of 3,287 adults with opioid use disorder. Some sub-analyses were completed on the sub-population of adults who received treatment (n = 923), and the subpopulation who reported a perceived unmet need for treatment (n = 408).

2.2.2 Measures

2.2.2.1 Exposure. The exposure of interest in the present study is the presence of at least one child (17 or younger) living in the household of the survey respondent at the time of the survey. Note that the NSDUH does not provide information about whether the adult respondent has any custodial responsibility for, or biological relationship to, any children in the household.

2.2.2.2 Study outcomes. The primary outcome was self-reported past-year use of any treatment for drugs or alcohol. Among those who reported receipt of any treatment, we examined treatment in specific settings: hospital, inpatient specialty program, outpatient specialty program, mental health center, emergency department, physician's office, jail or prison, and self-help group. Among those who reported receipt of any treatment, we also examined the reported payment source: insurance, savings, a family member or friend, or a court.

The second outcome of interest was perceived unmet need for treatment. This includes respondents who did not receive any treatment but reported they felt a need for treatment (for use of any substance), as well as respondents receiving treatment who reported they felt a need for additional treatment. Among those who reported a need for treatment, following Ali and colleagues (Ali, Teich, & Mutter, 2016) we examined five reasons for not receiving treatment: 1) <u>Financial barriers</u> included having no insurance or insurance not covering treatment; 2) <u>Access barriers</u> included having no transportation, not being able to find the right type of program, not being able to find a program with openings, or not knowing where to go; 3) <u>Stigma</u> included fearing that that others would know about drug use, that neighbors would have a negative opinion, or that treatment would have a negative effect on one's job; 4) <u>Not being a priority</u> included a report of not

needing help, not thinking treatment would help, or participants believing they could "handle it" without treatment; 5) A final reason was "<u>not ready to stop using</u>." The available items do not inquire about parent-specific barriers, such as inadequate childcare or fear of having dependent children removed from care.

2.2.2.3 Demographics. Demographic variables examined include age, sex, race/ethnicity, education level, employment status, urbanicity of residence, past-year presence of an alcohol use disorder, and past-year use of tobacco.

2.2.3. Analytic Approach

As a preliminary analysis, we present trends over time in use of substance use treatment and perceived need for substance use treatment, stratified by the presence of a child in the household. Then, adults living with children and adults living without children were compared on all outcomes using logistic regression. Unadjusted models were estimated, as well as models that adjusted for all demographic variables. Finally, past research on substance use treatment for adults with children has mostly focused on women (Greenfield et al., 2007), but the effect of the presence of a child on treatment use and need for treatment may differ by sex. We test this hypothesis explicitly by adding an interaction term between presence of a child in the household and sex in models for these two outcomes. Regression coefficients were, in all cases, exponentiated for interpretation as odds ratios – the relative odds of the outcome among adults living with children as compared to adults not living with children.

All estimates incorporated survey design elements – clustering, stratification, and weighting – and therefore can be considered representative of the United States population living in households during the 2010-2014 period. Standard errors and

corresponding 95% confidence Wald confidence intervals were estimated using Taylor series linearization. All analyses were conducted in R 3.4.3 (R Core Team, 2017) using the "survey" package (Lumley, 2004).

As a sensitivity analysis, we restricted the sample to adults 26 and older – who may be more likely to have caregiving responsibilities for children living in their household – and repeated the entire analysis.

2.3 Results

2.3.1 Demographics

Based on the nationally representative NSDUH data, we estimate that during the period from 2010 - 2014, approximately 2 million U.S. adults – just under 1 percent of all adults – met criteria for an opioid use disorder. Of these, approximately 820,000 (~41%) were living with at least one child. In the population with opioid use disorder, the demographics of adults living with children and adults living without children were somewhat different – adults with children were more likely to be between the ages of 26 and 50 than younger or older age groups, to be female, to have lower levels of education, and to live outside urban centers, and were less likely to have an alcohol use disorder. Detailed demographics are shown in Table 1.

2.3.2 Treatment

Among adults with an opioid use disorder living with children, an estimated 27.7 percent (95% CI 23.5% to 31.9 percent) reported receiving any substance use treatment in the past year. This rate was not significantly different from adults not living with a child (aOR: 0.91, 95% CI 0.79 to 1.18). Interaction tests suggest this null effect was the same for men and women (analysis not shown). There were no discernible trends over

time in the prevalence of treatment use, nor did trends differ between adults with children or adults without children (Figure 1).

Among those who were treated, the most common treatment settings were outpatient specialty treatment (60.2%, 95% CI 52.3% to 68.1%) and self-help groups (58.4%, 95% CI 51.5% to 65.4%). The most common source of financing for treatment was personal savings. The prevalence of treatment, treatment settings, and payers were similar between adults with children in the household and adults without children in the household, and there were no significant differences between groups in adjusted or unadjusted analyses.

2.3.3 Perceived Need for Treatment

About 14.8% (95% CI 10.8% to 18.9%) of adults living with a child reported a perceived unmet need for treatment or for additional treatment. There were no significant differences in perceived need between adults living with children and adults living with no children (aOR 1.17, 95% CI 0.73 to 1.88). Interaction tests suggest this null effect was the same for men and women (analysis not shown). There were no discernible trends over time in the prevalence of perceived need, nor did trends differ between adults with children or adults without children (Figure 1).

Among those with a perceived unmet need for treatment, by far the most commonly reported barrier to care was financial (60.8%, 95% CI 47.0% to 74.6%) – this was true for both adults with children and adults without children. Among those with perceived need, there were significant differences in barriers to care. After adjusting for all measured demographic factors, stigma (aOR 4.09, 95% CI 1.50 to 11.17), access barriers (aOR 2.90, 95% CI 1.19 to 7.07), and not believing that treatment should be a

priority (aOR 2.79, 95% CI 1.17 to 6.62) were all more common among adults living with children than among adults living without children. By contrast, adults living with children were less likely to report that they would not get treatment because they were "not ready to stop using" (aOR 0.39, 95% CI 0.19 - 0.8).

Detailed results are shown in Table 2. Results of the sensitivity analysis were qualitatively unchanged from the main analysis and are not shown.

2.4 Discussion

As recently as 2010-2014, approximately four in ten U.S. adults with an opioid use disorder – more than 800,000 people – lived in a household with a child. Not all of these adults are parents or would have custodial responsibilities (and that data is not available in the public access NSDUH). Nevertheless, it is likely that many are parents or caregivers. Even in cases where these adults do not have formal parental or caregiver relationships with children in their households, there are still pathways by which the presence of an adult with an opioid use disorder in the household could increase children's risk of harm, for example if drugs or drug paraphernalia are left unsecured (Kennedy-Hendricks et al., 2016), or if the participant introduces high risk partners into the social ecology of children (Barnard & McKeganey, 2004). This estimate does not even capture parents in inpatient or correctional settings. In summary, there is good reason to believe that the opioid epidemic is affecting hundreds of thousands of families and their children.

Moreover, adults with opioid use disorder living with children are demographically different from their counterparts living without children. Adults with opioid use disorders

who live with children are more likely to be women than their counterparts. Historically, women have been less likely to seek substance use treatment than men, and may have a different risk profile – including comorbid psychiatric disorders and a history of trauma – which would make them candidates for treatment in specialized settings (Greenfield et al., 2007). Adults with opioid use disorder who live with children are also more likely to live in rural areas where medication-assisted treatment for opioid use disorder is scarce, particularly special programs for pregnant or parenting women (Patrick & Schiff, 2017).

We found that fewer than three in ten adults with an opioid use disorder living with children reported receiving any form of treatment, suggesting a major unmet need for substance use treatment for families, comparable to that for adults living in households without children. Unfortunately, NSDUH offers no way of assessing the quality of treatments. Among those treated, the most common source of payment for treatment was personal savings. Again, this was true regardless of the presence of children in the household. Of note, patterns in treatment financing may have changed following the expansion of Medicaid under the 2014 Affordable Care Act, which substantially reduced the uninsured rate among adults with heroin use disorder and tripled the odds of treatment being paid for by insurance (Feder et al., 2017). In fact, Medicaid is the primary form of insurance coverage for adults with opioid use disorder (Feder et al., 2017), and other research suggests that acquiring Medicaid is associated with reduced unmet need for substance use disorder treatment (Wen, Druss, & Cummings, 2015); preserving and expanding Medicaid coverage is likely essential to expanding access to opioid use disorder treatment for families.

Contrary to our hypothesis, we found no difference in perceived unmet need for treatment between adults living with children and adults living without children. However, among those who perceived a need for treatment, there was some evidence that adults living with children were less likely to say they were "not ready to stop using." This is consistent with Barnard and colleagues' conclusion that living with a child is a motivator for adults to reduce or stop using illicit opioids (Barnard & McKeganey, 2004). Barnard and colleagues' research was conducted retrospectively in a sample that had received treatment. Taken together, our findings and their findings are consistent with the notion that living with a child is a motivation for people who have an opioid use disorder to try to change their behavior, but only among the minority who are aware that their opioid use is problematic.

Further, among those who perceived unmet treatment need, we also found that stigma was twice as likely to be reported as a barrier to treatment among adults living with children, and this effect rose to four times more likely after adjusting for demographic factors. Adults with children may fear that they will be judged by neighbors or peers to be bad parents if their substance use disorder is found out, or that their children will be removed from their care if they seek treatment for substance use disorders. Indeed, media representations of parents struggling with opioid addiction can be stigmatizing when taken out of context (Carissimo, 2016). Access barriers were also twice as common among adults living with children. This is consistent with other research which has found that access to transportation, availability of childcare, and trauma-informed programming play an important role in engaging parents and pregnant women in treatment (Neger & Prinz, 2015; Patrick & Schiff, 2017), although these

specific barriers were not assessed in the NSDUH survey. It is important to note that these between-group comparisons were estimated in a small sample of only 408 adults; the very wide confidence intervals suggest that these results be interpreted as preliminary. It is also important to note that financial barriers were the most important barrier to treatment for adults living with and without children. Addressing financial barriers is probably the most important strategy for increasing utilization of substance use treatment for both groups.

This study has a number of limitations. First, there is evidence that, prior to 2015, the NSDUH undercounted opioid use disorders among people who were taking opioids longterm as prescribed by a doctor. This is a significant limitation, because there is some evidence that as many as a third of this population would meet criteria for a use disorder, and risk for overdose in this population is still high (Boscarino et al., 2011; Kolodny et al., 2015). Second, the NSDUH only captures individuals in households; people who use opioids illicitly are likely overrepresented in marginalized populations such as homeless or incarcerated persons who will not be captured in the NSDUH. Therefore, any trends we identify should be understood to be representative only of the population living in households. Third, data from 2010-2014 may not be representative of the current state of the opioid epidemic, which has grown more severe even in the last few years (National Institute on Drug Abuse, 2017). Fourth, this study focuses on adults living with a child in the household. These adults may or may not be parents, nor do they necessarily have caregiving responsibilities. Conversely, those adults who are not living with a child in the household may be parents or caregivers to children who do not live in the household, for example if their children have been placed in foster care or have simply moved out. Our

sensitivity analysis restricted to adults over 25 – who may be more likely to have caregiving responsibilities – did not change the results. However, future research should examine the needs of parents and caregivers specifically. Fifth, lack of detail in the NSDUH's measures of treatment and treatment barriers to care make findings difficult to interpret. In particular, there is no way to know what percentage of treatment is medication-assisted – the highest standard of care for opioid use disorder – and important barriers to substance use treatment for parents such as lack of childcare were not assessed. Finally, the data used in this analysis are cross-sectional which limits causal inference regarding the association between living with children and self-reported barriers to care

2.5 Conclusion

This study is the first to examine, on a national scale, the treatment needs of adults struggling with opioid use disorder while living with minor children. We show that more than four out of every ten adults with an opioid use disorder are living with children, and that most of these adults are not receiving any treatment in a one-year period. Expanding access to treatment – in particular, medication-assisted treatment – for all people with opioid use disorder has been identified as an essential strategy for addressing the current epidemic (National Institute on Drug Abuse, 2017). Yet, for the most part, the needs of children and families in the opioid epidemic have not been a focus of research or policy. For example, in a recent New York Times survey of how 30 drug policy experts would prioritize investments in combatting the opioid epidemic, there was no mention of specialized services for children or families (Katz, 2018). Our findings suggest that

efforts to expand opioid use disorder programs must include investment in programs that meet the specialized needs of families.

Further, our findings offer preliminary evidence that stigma is a uniquely important to deterrent to treatment for adults with an opioid use disorder who live with children. Researchers, care providers, and the media must employ best practices when communicating about opioid use disorder, particularly when children and families are discussed (Feder & Krawczyk, 2017). While our study shows that many adults with opioid use disorder live with a child, communications that create the perception that addiction is a moral failing, that suggest children are necessarily and irreparably harmed by their parents' substance use, and that obfuscate the benefit of effective treatment, may indirectly keep these adults from seeking the treatment they need to keep themselves and their children healthy.

2.6 References

- Ali, M. M., Teich, J. L., & Mutter, R. (2015). The role of perceived need and health insurance in substance use treatment: implications for the Affordable Care Act. *Journal of Substance Abuse Treatment*, 54, 14–20.
- Ali, M. M., Teich, J. L., & Mutter, R. (2016). Reasons for Not Seeking Substance Use Disorder Treatment: Variations by Health Insurance Coverage. *The Journal of Behavioral Health Services & Research*, 1–12.
- Anda, R. F., Felitti, V. J., Bremner, J. D., Walker, J. D., Whitfield, C. H., Perry, B. D., ... Giles, W. H. (2006). The enduring effects of abuse and related adverse experiences in childhood. *European Archives of Psychiatry and Clinical Neuroscience*, 256(3), 174–186.
- Andersen, R. M. (1995). Revisiting the behavioral model and access to medical care: does it matter? *Journal of Health and Social Behavior*, 1–10.
- Barnard, M., & McKeganey, N. (2004a). The impact of parental problem drug use on children: what is the problem and what can be done to help? *Addiction*, 99(5), 552–559.
- Barnard, M., & McKeganey, N. (2004b). The impact of parental problem drug use on children: what is the problem and what can be done to help? *Addiction*, 99(5), 552–559.
- Carissimo, J. (2016, September 14). Four-year-old boy pictured in car with parents overdosed on heroin finds new home. Retrieved March 15, 2018, from http://www.independent.co.uk/news/world/americas/heroin-overdose-parents-carphoto-boy-finds-new-home-ohio-a7307391.html

- Center for Behavioral Health and Quality Statistics. (2015). National Survey on Drug Use and Health: 2014 and 2015 Redesign Changes. Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data/sites/default/files/NSDUH-RedesignChanges-2015.pdf
- Christie, G. C., Baker, C. G. C., Cooper, G. R., Kennedy, C. P. J., Madras, B., & Bondi,F. A. G. P. (n.d.). THE PRESIDENT'S COMMISSION ON COMBATINGDRUG ADDICTION AND THE OPIOID CRISIS.
- Dawe, S., & Harnett, P. (2007). Reducing potential for child abuse among methadonemaintained parents: Results from a randomized controlled trial. *Journal of Substance Abuse Treatment*, 32(4), 381–390.
- Dube, S. R., Felitti, V. J., Dong, M., Chapman, D. P., Giles, W. H., & Anda, R. F. (2003). Childhood abuse, neglect, and household dysfunction and the risk of illicit drug use: the adverse childhood experiences study. *Pediatrics*, *111*(3), 564–572.

European Monitoring Center for Drugs and Drug Addiction. (2012). Pregnancy,
Childcare and the Family: Key Issues for Europe's Response to Drugs.
Publications Office of the European Union. Retrieved from
http://www.emcdda.europa.eu/system/files/publications/671/TDSI12001ENC_39
6469.PDF

Feder, K. A., & Krawczyk, N. (2017, August). Four facts every journalist should know when covering the opioid epidemic. *Columbia Journalism Review*. Retrieved from https://www.cjr.org/united_states_project/opioid-journalist-advice.php

Feder, K. A., Mojtabai, R., Krawczyk, N., Young, A. S., Kealhofer, M., Tormohlen, K.

N., & Crum, R. M. (2017). Trends in insurance coverage and treatment among persons with opioid use disorders following the Affordable Care Act. *Drug and Alcohol Dependence*, *179*, 271–274.

- Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V.,
 ... Marks, J. S. (1998). Relationship of childhood abuse and household
 dysfunction to many of the leading causes of death in adults: The Adverse
 Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine*, 14(4), 245–258.
- Ghertner, R., Baldwin, M., Crouse, G., Radel, L., & Waters, A. (2018). The relationship between substance use indicators and child welfare caseloads. *ASPE*. Retrieved from

https://aspe.hhs.gov/system/files/pdf/258831/SubstanceUseCWCaseloads.pdf

- Greenfield, S. F., Brooks, A. J., Gordon, S. M., Green, C. A., Kropp, F., McHugh, R. K.,
 ... Miele, G. M. (2007). Substance abuse treatment entry, retention, and outcome in women: A review of the literature. *Drug and Alcohol Dependence*, 86(1), 1–21.
- Grella, C. E., Needell, B., Shi, Y., & Hser, Y.-I. (2009). Do drug treatment services predict reunification outcomes of mothers and their children in child welfare? *Journal of Substance Abuse Treatment*, 36(3), 278–293.
- Hall, M. T., Wilfong, J., Huebner, R. A., Posze, L., & Willauer, T. (2016). Medication-Assisted Treatment Improves Child Permanency Outcomes for Opioid-Using Families in the Child Welfare System. *Journal of Substance Abuse Treatment*, *71*, 63–67.
- Jones, C. M., Campopiano, M., Baldwin, G., & McCance-Katz, E. (2015, July 9).

National and State Treatment Need and Capacity for Opioid Agonist Medication-Assisted Treatment [research-article]. https://doi.org/10.2105/AJPH.2015.302664

- Kane, J. M., Colvin, J. D., Bartlett, A. H., & Hall, M. (2018). Opioid-Related Critical Care Resource Use in US Children's Hospitals. *Pediatrics*, e20173335. https://doi.org/10.1542/peds.2017-3335
- Katz, J. (2018, February 14). How a Police Chief, a Governor and a Sociologist Would Spend \$100 Billion to Solve the Opioid Crisis - The New York Times. Retrieved February 19, 2018, from https://www.nytimes.com/interactive/2018/02/14/upshot/opioid-crisissolutions.html
- Kennedy-Hendricks, A., Gielen, A., McDonald, E., McGinty, E. E., Shields, W., & Barry, C. L. (2016). Medication sharing, storage, and disposal practices for opioid medications among US adults. *JAMA Internal Medicine*, *176*(7), 1027–1029.
- Kolar, A. F., Brown, B. S., Haertzen, C. A., & Michaelson, B. S. (1994). Children of substance abusers: The life experiences of children of opiate addicts in methadone maintenance. *The American Journal of Drug and Alcohol Abuse*, 20(2), 159–171.
- Krawczyk, N., Feder, K. A., Fingerhood, M. I., & Saloner, B. (2017). Racial and ethnic differences in opioid agonist treatment for opioid use disorder in a U.S. national sample. *Drug and Alcohol Dependence*, *178*, 512–518. https://doi.org/10.1016/j.drugalcdep.2017.06.009

Lamont, A. (2010). Effects of child abuse and neglect for children and adolescents.

Lumley, T. (2004). Analysis of complex survey samples. *Journal of Statistical Software*, *9*(1), 1–19.

- Mayes, L. C., Feldman, R., Granger, R. H., Haynes, O. M., Bornstein, M. H., & Schottenfeld, R. (1997). The effects of polydrug use with and without cocaine on mother-infant interaction at 3 and 6 months. *Infant Behavior and Development*, 20(4), 489–502.
- National Institute on Drug Abuse. (2017, September 15). Overdose Death Rates. Retrieved February 19, 2018, from https://www.drugabuse.gov/relatedtopics/trends-statistics/overdose-death-rates
- Neger, E. N., & Prinz, R. J. (2015). Interventions to address parenting and parental substance abuse: Conceptual and methodological considerations. *Clinical Psychology Review*, 39, 71–82.
- Patrick, S. W., & Schiff, D. M. (2017). A Public Health Response to Opioid Use in Pregnancy. *Pediatrics*, e20164070.
- Quast, T., Storch, E. A., & Yampolskaya, S. (2018). Opioid Prescription Rates And Child Removals: Evidence From Florida. *Health Affairs*, 37(1), 134–139. https://doi.org/10.1377/hlthaff.2017.1023
- R Core Team. (2017). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from https://www.Rproject.org/

Radel, L., Baldwin, M., Crouse, G., Ghertner, R., & Waters, A. (2018). Substance use,
the opioid epidemic, and the child welfare system: Key Findings from a Mixed
Methods Study. ASPE. Retrieved from
https://aspe.hhs.gov/system/files/pdf/258836/SubstanceUseChildWelfareOvervie
w.pdf

- Roddy, J., & Greenwald, M. (2009). An economic analysis of income and expenditures by heroin-using research volunteers. *Substance Use & Misuse*, 44(11), 1503–1518.
- Ryan, S. A., Gonzalez, P. K., Patrick, S. W., Quigley, J., Siqueira, L., & Walker, L. R. (2016). Medication-assisted treatment of adolescents with opioid use disorders. *Pediatrics*, 138(3), e20161893.

SAMHSA. (n.d.). SAMHDA. Retrieved from https://www.datafiles.samhsa.gov/

- Volkow, N. D., Frieden, T. R., Hyde, P. S., & Cha, S. S. (2014). Medication-assisted therapies—tackling the opioid-overdose epidemic. *New England Journal of Medicine*, 370(22), 2063–2066.
- Wellisch, D. K., & Steinberg, M. R. (1980). Parenting attitudes of addict mothers. International Journal of the Addictions, 15(6), 809–819.
- Wen, H., Druss, B. G., & Cummings, J. R. (2015). Effect of Medicaid Expansions on Health Insurance Coverage and Access to Care among Low-Income Adults with Behavioral Health Conditions. *Health Services Research*, 50(6), 1787–1809.
- Wolf, J. P., Ponicki, W. R., Kepple, N. J., & Gaidus, A. (2016). Are community level prescription opioid overdoses associated with child harm? A spatial analysis of California zip codes, 2001–2011. Drug and Alcohol Dependence, 166, 202–208.

	All	Child In Household	No Child in Household	
Population	1,987,673	815,849	1,171,824	
	Percent (95% CI)	Percent (95% CI)	Percent (95% CI)	
Age				
18-25	31.9 (29.3 - 34.5)	30 (26.9 - 33.1)	33.2 (29.6 - 36.8)	
26-34	30.7 (27.7 - 33.7)	35.2 (29.9 - 40.5)	27.6 (23.8 - 31.4)	
35-49	21.1 (18.2 - 24.1)	26.7 (22.2 - 31.2)	17.3 (13.7 - 20.9)	
50-64	13.9 (10.4 - 17.3)	6.3 (2.0 - 10.6)	19.1 (14.2 - 24.0)	
65+	2.4 (0.8 - 3.9)	1.8(0.0 - 4.4)	2.8 (0.8 - 4.8)	
Sex		· · · · · ·		
Male	60.5 (57.0 - 64.0)	54.7 (50.1 - 59.3)	64.5 (59.9 - 69.1)	
Female	39.5 (36.0 - 43.0)	45.3 (40.7 - 49.9)	35.5 (30.9 - 40.1)	
Race/Ethnicity		×		
White	72 (68.9 - 75.1)	69.2 (64.1 - 74.2)	74 (69.8 - 78.3)	
Black	9.9 (7.7 - 12)	9 (5.9 - 12)	10.5 (7.4 - 13.7)	
Hispanic	12.9 (10.4 - 15.4)	16 (11.9 - 20.1)	10.8 (7.8 - 13.8)	
Other	5.1 (3.8 - 6.5)	5.9 (3.7 - 8.1)	4.6 (2.9 - 6.3)	
Education Level				
Less than High School	23.8 (20.8 - 26.8)	28.3 (23.5 - 33.1)	20.6 (17.5 - 23.8)	
High School	34.6 (31.5 - 37.6)	37.3 (32.4 - 42.3)	32.6 (28.3 - 37)	
Some College	30.7 (27.5 - 34)	25.5 (22.1 - 28.8)	34.4 (29.4 - 39.4)	
College	10.9 (9.3 - 12.6)	8.9 (6.5 - 11.3)	12.3 (9.9 - 14.8)	
Employment Status				
Full Time	41.4 (37.6 - 45.1)	43.6 (38.4 - 48.8)	39.8 (35.3 - 44.3)	
Part Time	16 (13.5 - 18.6)	14.4 (11.8 - 17.0)	17.2 (13.4 - 21.0)	
Unemployed	14.8 (12.8 - 16.7)	16.8 (13.7 - 19.9)	13.4 (11.1 - 15.7)	
Other	27.8 (24.7 - 31.0)	25.2 (21.1 - 29.3)	29.7 (25.1 - 34.3)	
Urbanicity		×		
Large Metro	53.8 (50.8 - 56.8)	49.5 (45.4 - 53.6)	56.9 (52.9 - 60.8)	
Small Metro	31.4 (28.6 - 34.3)	31.2 (26.7 - 35.6)	31.6 (28.1 - 35.2)	
Non-Metro	14.7 (12.6 - 16.8)	19.4 (15.8 - 23.0)	11.5 (8.9 - 14.1)	
Comorbid Substance Use		×	```'	
Alcohol Use Disorder	36.1 (33.2 - 38.9)	31.6 (28 - 35.3)	39.1 (35 - 43.3)	
Past-Year Cigarette Use	78.4 (75.1 - 81.7)	76.5 (71.3 - 81.6)	79.8 (75.8 - 83.7)	

	2.7 Exhibits	
Table 2.1. Characteristics of U.S.	Adults with Opioid Use Disorder, 2010-2014	

Table 2.2. Association of Treatment Characteristics with Presence of Child in Househo	old
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	All	Child in	No Child in	Unadjusted Odds	Adjusted Odds
		Household	Household	Ratio	Ratio
	Percent (95% CI)	Percent (95% CI)	Percent (95% CI)	OR (95% CI)	OR (95% CI)
Any Past Year Treatment	29.6 (26.3 - 33)	27.7 (23.5 - 31.9)	31.0 (26.7 - 35.2)	0.85 (0.66 - 1.11)	0.91 (0.7 - 1.18)
Treatment Location (% of Treated)					
Hospital	41.8 (36.4 - 47.1)	36.1 (27.2 - 45.0)	45.3 (38.1 - 52.5)	0.68 (0.41 - 1.14)	0.79 (0.45 - 1.39)
Inpatient	47.8 (42.5 - 53)	42.8 (34.5 - 51.1)	50.9 (43.5 - 58.2)	0.72 (0.45 - 1.17)	0.75 (0.45 - 1.26)
Outpatient	56.2 (50.8 - 61.7)	60.2 (52.3 - 68.1)	53.8 (46.4 - 61.1)	1.3 (0.83 - 2.05)	1.6 (1 - 2.57)
Mental Health Center	34.4 (29.5 - 39.3)	34.6 (27.7 - 41.6)	34.3 (27.4 - 41.1)	1.02 (0.65 - 1.58)	1.03 (0.63 - 1.66)
Emergency Department	28.6 (23.5 - 33.7)	25.8 (18.8 - 32.9)	30.4 (23.7 - 37.1)	0.8 (0.49 - 1.29)	1.09 (0.59 - 2)
Physician's Office	31.5 (26.1 - 36.9)	35.3 (27.9 - 42.8)	29.2 (21.6 - 36.7)	1.33 (0.81 - 2.18)	1.46 (0.88 - 2.41)
Jail or Prison	11.7 (8.0 - 15.5)	9.1 (4.4 - 13.9)	13.3 (7.9 - 18.8)	0.65 (0.3 - 1.42)	0.76 (0.33 - 1.77)
Self Help Group	61.6 (57.1 - 66.2)	58.4 (51.5 - 65.4)	63.7 (57.3 - 70)	0.8 (0.53 - 1.22)	1.01 (0.61 - 1.67)
Payment Source (% of Treated)					
Insurance	39.1 (33.3 - 44.9)	39.9 (32.2 - 47.7)	38.6 (30.9 - 46.3)	1.06 (0.68 - 1.65)	0.94 (0.58 - 1.51)
Savings	46.3 (40.3 - 52.3)	51.5 (44.1 - 58.9)	43 (34.8 - 51.1)	1.41 (0.91 - 2.17)	1.26 (0.83 - 1.93)
Family or Friend	33.4 (27.5 - 39.3)	33.7 (24.9 - 42.4)	33.2 (25.6 - 40.8)	1.02 (0.61 - 1.71)	1.18 (0.66 - 2.09)
Court	7.0 (4.1 - 10.0)	5.9 (2.7 - 9.1)	7.7 (3.4 - 12.1)	0.75 (0.33 - 1.73)	0.89 (0.39 - 2.03)
Perceived Need for Treatment	13.9 (11.8 - 15.9)	14.8 (10.8 - 18.9)	13.2 (10.8 - 15.6)	1.15 (0.76 - 1.72)	1.17 (0.73 - 1.88)
Barriers (% of Persons with Perceived Need)	```'	```'	```		```'
Financial	55.9 (47.1 - 64.6)	60.8 (47 - 74.6)	52 (42.3 - 61.8)	1.43 (0.73 - 2.8)	0.96 (0.51 - 1.82)
Access	25.4 (16.1 - 34.6)	34.9 (18.7 - 51.1)	17.9 (11.3 - 24.6)	2.45 (1.1 - 5.46)	2.9 (1.19 - 7.07)
Stigma	27.1 (19.2 - 35.1)	37.3 (22.6 - 52)	19.2 (11.3 - 27.1)	2.51 (1.09 - 5.79)	4.09 (1.5 - 11.17)
Not Ready to Stop Using	23.3 (17.7 - 29.0)	14 (6.6 - 21.3)	30.7 (22.7 - 38.7)	0.37 (0.17 - 0.8)	0.39 (0.19 - 0.8)
Not Priority	9.7 (4.9 - 14.6)	13.3 (3.9 - 22.7)	6.9 (3.2 - 10.7)	2.06 (0.78 - 5.43)	2.79 (1.17 - 6.62)

Note: Adjusted odds ratios adjusted for age, sex, race/ethnicity, education, employment, urbanicity, presence of an alcohol use disorder in the past year, and past year cigarette use.

Note: Odds ratios statistically significant at the p<.05 level are bolded.

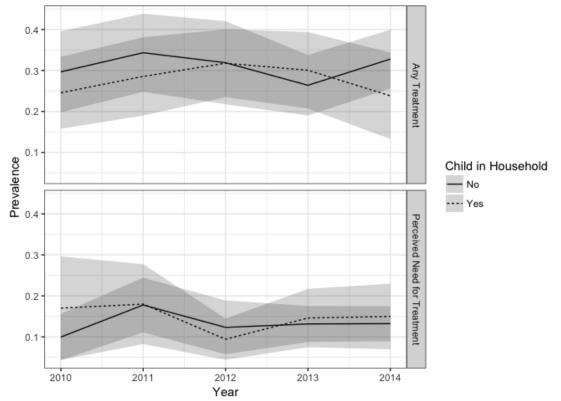


Figure 2.1. Treatment Use and Perceived Need for Treatment by Presence of Child in Household, U.S. Adults with Opioid Use Disorder, 2010-2014

CHAPTER 3. COMMON TRAJECTORIES OF HEROIN AND COCAINE USE OVER THE LIFE COURSE: A 30-YEAR COHORT STUDY OF PEOPLE WHO INJECT DRUGS, 1988-2018

3.0 Abstract

Background: Substance misuse disorders and overdose are a leading cause of morbidity and mortality among U.S. adults. Substance misuse behaviors are known to be chronic, but their course is not well characterized over the life span, especially among persons not in treatment.

Methods: Data come from ALIVE, a longitudinal cohort under observation since 1988 with community-based recruitment of 2,845 adults from the Baltimore area who currently inject or formerly injected drugs. Past six-month heroin and cocaine use by any route of administration were assessed at twice-annual study visits conducted between 1988 until 2016. Latent class linear mixed models were used to identify and describe common trajectories of use for each these drugs over the life course.

Results: Female participants attended 29% of visits, and Black participants attended 93%. Heroin and cocaine use were reported at 47% and 49% of visits respecitively. In single-class models, the predicted probabilities of past six-month use declined gradually from 67% and 69% at age 30 to 23% and 22% by age 60 for heroin and cocaine respectively. Latent class models revealed up to six common trajectories of use for both heroin and cocaine, with very similar class structures. In particular, for both drugs, sub-groups include three "cessation" trajectories that decline to zero probability of use; a diminishing trajectory with declining probability of use that does not reach zero by age 60; a relapsing trajectory with risk hovering around 50% over the entire period from age 30 to 60; and an "accelerating" trajectory with low risk of use in midlife but high risk of relapse in later life. **Conclusion:** The course of heroin and cocaine use over an extended period of adult life is heterogeneous among people who inject drugs. Future research on this heterogeneity can inform long-term management and differentiation of treatment for adults who use heroin or cocaine.

3.1 Introduction

The United States is currently experiencing an unprecedented epidemic of drugrelated problems. In 2017, an estimated 72,000 Americans died from a drug overdose (National Institute on Drug Abuse, 2018). This increase in drug-involved deaths was primarily caused by deaths from opioid drugs, including synthetic opioids like fentanyl, heroin, and prescription opioid pain-relievers. In addition, cocaine-related deaths have increased sharply (Seth, 2018), an increase that likely reflects increases in the use of cocaine mixed with fentanyl-like drugs (Miller, Stogner, Miller, & Blough, 2017). Opioid-related inpatient hospital admissions have increased (Healthcare Cost and Utilization Project (HCUP), 2018), as have cases of opioid use in pregnancy and related birth complications (Patrick et al., 2012). These increases in drug-related problems were so dramatic that they were a primary contributor to an overall declines in life expectancy in the United States (Associated Press, 2018; Murphy, Xu, Kochanek, & Arias, n.d.).

While acute health problems like overdose deaths have received most research and media attention, by 2016, 2.1 million Americans were living with an opioid use disorder and 960,000 were living with a cocaine use disorder (Ahrnsbrak, Bose, Hedden, Lipari, & Park-Lee, 2017). Substance use disorders are chronic conditions characterized by periods of remission and relapse and frequent comorbidity with other physical and mental health problems (McLellan, Lewis, O'Brien, & Kleber, 2000; Saitz, Larson, LaBelle, Richardson, & Samet, 2008). This has motivated support for addressing substance use disorders through a chronic disease management approach over the life course, similar to diseases like diabetes (Saitz et al., 2008). Further, having a use disorder is a major risk factor for drug-involved death (Kolodny et al., 2015), and effective

addiction treatment must be a cornerstone of addressing the overdose crisis (Christie et al., n.d.; Kolodny et al., 2015). To meet the needs of a growing number of Americans living with substance use disorder, research is needed to understand the long-term progress of opioid use and other drug use in people with opioid use disorder over the course of adult life.

Research on the course of substance use disorders, and opioid use disorder in particular, is limited. A number of long-term cohort studies have followed heroin users over a long period of time. These studies are consistent in finding that attempts to cease heroin use are common but most people relapse at some point; co-occurring physical and mental health problems are the norm, not an exception; risk for illicit use is lowest when participants receive medication assisted treatment, for example for with buprenorphinenaloxone; and mortality rates in this population are very high, particularly during periods of active use when overdose death is the leading cause of death (Haastrup & Jepsen, 1988; Hser, Hoffman, Grella, & Anglin, 2001; Price, Risk, & Spitznagel, 2001; Robins & Slobodyan, 2003; Weiss et al., 2011). Most of these studies are limited by unique samples, for example of people in treatment or of Vietnam War veterans.

Further, most of the existing studies look for trajectories of behavior common to the whole population. Instead, there may be subtypes of users or people with use disorder who experience different trajectories of use over different stages of life. Identifying these subgroups is challenging, because, as with most behavioral disorders, there are no biomarkers to distinguish members of one subtype from another. Instead, two studies have used latent variable methods to parse out latent subgroups of heroin users. First, Hser and colleagues followed a sample of 471 male heroin users from a California

treatment program for fifteen years following first use. They identified three types of users – a group of early quitters, a group of stable high users, and a group of "decelerated" users whose use declined after a decade, but never ceased (Hser, Huang, Chou, & Anglin, 2007). Second, Genberg and colleagues (Genberg et al., 2011) followed a cohort of 1,700 people living in Baltimore recruited into a longitudinal cohort study of people who injected drugs (mostly heroin users) over a 20-year period from their time of entry into the study. They identified five common trajectories of injection drug use – early, delayed, and late cessation groups, a relapsing group, and a group of sustained users who made up about a third of the sample.

This study builds on the work of Genberg and colleagues. We use ten additional years of data from the same active cohort study, and focused on participant age, rather than time since entry. We also explore distinct trajectories of use of two specific drugs – heroin and cocaine – rather than injecting behavior generally. With thirty years of data combined from six recruitment periods, we can characterize the trajectories of use for these drugs over an extended period of the adult life in a community-based sample and explore differences in the course of heroin and cocaine use.

3.2 Materials and Methods

3.2.1 Study Participants

Study participants come from the AIDS Linked to the Intravenous Experience (ALIVE) study, an active, community-based, prospective cohort study of adults living in and around Baltimore City, Maryland. In 1988, 2,946 participants who had injected drugs in the prior 10 years were recruited to study the natural history of HIV (Vlahov et al., 1991). Additional waves of recruitment were conducted in 1994-1995 1998, 2000, 2005-

2008, and 2015-2018 to replenish the original sample; later recruitment waves required participants to have injected drugs at least once in the past year (as opposed to in the past 10 years as for the original recruitment). Participants attend twice annual study visits where they complete a physical exam, standardized interviewer-administered and audio-computer assisted surveys about drug use and related behaviors, and provide a blood sample for HIV testing. Once enrolled, participants remain in the ALIVE cohort until they die, choose to exit the study, or are lost to follow up. The Johns Hopkins University Institutional Review Board approved the study and all participants provided informed written consent. Details of ALIVE are described elsewhere (Vlahov et al., 1991).

The present analysis used data from all ALIVE participants who attended at least four study visits between in May of 1988 and December of 2016. Of the original sample of 60,137 study visits, 1,541 visits were excluded because data on either heroin or cocaine use were missing, and another 2,114 because participants had been in follow-up for fewer than four total visits at the time of analysis. This left a final sample of 2,845 participants who contributed 56,482 study visits. The median number of visits contributed by a participant was 16 (IQR 9 visits to 28 vsitis). This sample was used in the main analysis of both heroin and cocaine outcomes.

The median time between study visits was 183 days (IQR 179 days to 202 days). Participants are eligible to remain in ALIVE until death, and may go extended periods without attending study visits. In this sample, the longest period between two study visits was under 415 days for 50% of the sample and 1,427 days for 90% of the sample; the longest gap between study visits in our sample was 25 years (see Limitations for further discussion of missing data).

3.2.2 Measures

Two outcomes were assessed in this analysis: 1) Past six-month heroin use by any route of administration assessed in ALIVE (including injecting heroin alone, snorting heroin alone, smoking heroin alone, and injecting heroin and cocaine simultaneously); and 2) Past six-month cocaine use by any route of administration assessed in ALIVE (including injecting cocaine alone, snorting cocaine, smoking crack cocaine, and injecting heroin and cocaine simultaneously). All outcomes were assessed via self-report in response to audio-computer-assisted-survey instruments (ACASI).

The primary independent variable was age in days. We adjusted for a small number of other covariates – demographic variables including sex (male, female) and race (black, white); and study-specific variables including decade of study visit (1980s, 1990s, 2000s, 2010s) and recruitment cohort (initial 1988 recruitment, or all other cohorts). This limited set of time-invariant covariates was selected because the goal of the study was to describe the natural history of drug use over the life course by estimating the probability of use as a function of age. Adjusting for other, time-varying covariates would be adjusting for mediators, and would bias the estimated association of age with drug use.

Finally, mortality and date of death for each participant was obtained from the National Death Index (NDI) with confirmation from death certificates.

3.3.3 Analytic Approach

The analysis was conducted separately for each of the two outcomes, but the approach was the same for both outcomes. Therefore, the "Approach" section refers generally to the outcome variable as "drug use."

3.2.3.1 Single Class Model. We first estimated the conditional probability of drug use as a function of age using generalized linear models with a probit link. We included linear and quadratic age terms, to allow for non-linear trends over time. Models adjusted for sex, race, study visit decade, and recruitment cohort. Random intercepts were used to account for the fact that repeated observations on the same participant are correlated. The mean estimated conditional probability of drug use was estimated and plotted as a function of age for ages 30 through 60 (approximately 95% of study visits fell in this range); for a hypothetical male Black participant (the most common demographic); recruited in cohorts other than the initial 1988 recruitment (i.e. more recent recruitments); attending a study visit in the 2010s (to make inference more relevant to the present day); and with a random intercept of 0.

3.2.3.2 Multiple Class Models. The goal of the main analysis was to identify subgroups of users who share a similar pattern of drug use over the life course. To do this, we used latent class linear mixed models (also known as growth mixture models). These models extend the regression conducted in the preliminary analysis to accommodate the possibility of two or more sub-populations (or "latent classes") of drug users, each with its own set of model parameters (Proust-Lima, Philipps, & Liquet, 2015). Specifically, the latent class linear mixed model assumes that each study participant is a member of exactly one of a finite number of classes, but this class status is unknown. The proportion of the population in each class, and the set of parameters associated with each class, are estimated simultaneously. In this analysis, only coefficients for the linear and quadratic age terms were allowed to differ across classes. All other parameters – all other regression coefficients, the regression intercept, and the random intercept variance – were

constrained to be the same for every class. Forcing the regression intercept to be the same across classes was used to impose the constraint that the conditional probability of use at age 20 was the same for all classes. This assumption reflects the fact that all participants were recruited based on their history of drug use, and prevents estimation of unrealistic classes with a very low probability of drug use at the beginning of adulthood.

We estimated models with 2, 3, 4, 5, and 6 classes. The model that best fit the data – as indicated by Akaike Information Criteria (AIC) and Bayesian Information Criteria (BIC) – was chosen for presentation and analysis. For that best-fitting model, as with the one-class models, the mean estimated conditional probability of drug use in each class was plotted as a function of age for ages 30 through 60, for a hypothetical male Black participant; recruited in waves other than the initial 1988 recruitment; attending a study visit in the 2010s; and with a random intercept of 0. We also name each class to qualitatively describe its trajectory, and present the proportion of the sample estimated to belong to each class.

3.2.3.3. Sensitivity Analyses -- Participants Surviving to 2016. Mortality rates in the ALIVE cohort are high – 49% of study participants contributing 40% of all study visits were deceased by the end of the observation period. This means that modeled trajectories of drug use at older ages increasingly reflect only the behavior of participants who will have survived to that point. For this reason, the entire analysis was repeated on a sample of participants still living at the end of the observation period (33,229 observations of 1,421 participants), to see if common trajectories of use are similar in drug users who survive.

3.2.3.4 Inference. All predicted probabilities are presented with 95% Wald confidence intervals. Statistical significane of regression coefficients is assessed at the p<.05 level with t-tests.

3.2.3.5 Software. All analyses were conducted in R 3.5.0 using the "lcmm" package (Proust-Lima et al., 2015). The lcmm package uses a Marquardt algorithm – a Newton-Raphson-like algorithm – to find maximum likelihood estimates and standard errors for all parameters. For multi-class models, multiple sets of random starting values were used to decrease the chance of models converging to a local, rather than global, maximum likelihood.

3.3 Results

3.3.1 Sample Characteristics

Past-six-month heroin use was reported at 47 percent of study visits, and past sixmonth cocaine use at 49 percent of study visits. The median age was 44.7 years. Half of all study visits came from participants between ages 38 and 51, and 90% came from participants between the ages of 30 and 60. The minimum age at any study visit was 19 years, and the maximum 81 years. Seventy-one percent of study visits had a male participant, and 93% had a Black participant. Approximately 33% of visits came from participants who were recruited at some time other than the initial recruitment conducted in 1988. Approximately 5% of visits were attened in the 1980s, 44% in the 1990s, 31% in the 2000s, and 20% in the 2010s.

3.3.2 Single-Class Model

In general, the predicted probability of both heroin and cocaine use declined steadily with age.

3.3.2.1 Heroin. The conditional predicted probability of past six-month heroin use at age 30 - for a male, Black participant, from the later recruitment waves, attending a study visit in the 2010s, with a random intercept of zero – was 66.5%. This declined to 53.3% by age 40, 38.2% by age 50, and 23.4% by age 60 (Figure 1).

3.3.2.2 Cocaine. The conditional predicted probability of past six-month heroin use at age 30 - for a male, Black participant, from the later recruitment waves, attending a study visit in the 2010s, with a random intercept of zero – was 68.6%. This declined to 54.5% by age 40, 38.0% by age 50, and 22.3% by age 60 (Figure 1).

3.3.3 Model Selection

Table 2 shows log-likelihood, AIC, and BIC statistics for two- through six-class models, for both heroin and cocaine use. For both outcomes, six-class models had the lowest AIC and BIC, suggesting these models best fit the data, and that the simple trajectory described above may actually average over as many as six different common latent subtypes of people who use heroin and cocaine respectively who experience different trajectories of use over the life course.

3.3.4 Best-Fitting Model

3.3.4.1 Heroin. Figure 1 shows the declining risk of heroin use over the life course disaggregated into six latent trajectories. There are three "cessation" trajectories, characterized by a high probability of use at age 30 eventually reaching zero probability of use by a user's late 30s (10%), mid-40s (11%), or mid-50s (24%). A fourth group of "diminishing" users (24%) also experienced consistent declining average probability of use over the life course, but that probability did not reach zero by age 60. A fifth group of "relapsing" users experienced relatively steady moderate probability of use (22%).

Finally, the sixth group of users (10%) had an "accelerating" probability of use that increased over the life course.

3.3.4.2 Cocaine. Figure 2 shows the declining risk of cocaine use over the life course disaggregated into six latent trajectories. There are three "cessation" trajectories, characterized by eventually reaching zero probability of use by a user's early early-30s (5%), early-40s (13%), and early-50s (18%). A fourth group of "diminishing" users (29%) also experienced consistent declining average probability of use over the life course, but that probability did not quite reach zero by age 60. A fifth group of "relapsing" users experienced relatively steady moderate probability of use (27%). Finally, the sixth group of users (9%) had had an "accelerating" probability of use that increased over the life course.

3.3.5 Other Covariates

The predicted trajectories shown are for a male, Black participant, recruited after the initial 1988 recruitment, attending a study visit in the 2010s (Table 1). Probit regression coefficients from the best-fitting six class model show race, gender, recruitment cohort, and visit era were all significantly associated with both heroin and cocaine use.

3.3.5.1 Heroin. All other characteristics held equal, female participants had significantly lower probability of heroin use than male participants (B = -0.31, p = <.001), Black participants had significantly higher probability of heroin use than White participants (B = 0.35, p = .002), participants recruited after 1988 had significantly higher probability of heroin use than participants recruited in 1988 (B = 0.84, p < .001), and

study visits in the 1990s (B = -.23, p <.001), 2000s (B = -.71, p<.001), and 2010s (B - 1.27, p<.001) had successively lower rates of heroin use than visits in the 1980s.

3.3.5.2 Cocaine. All other characteristics held equal, female participants had significantly lower probability of cocaine use than male participants (B = -0.16, p = .003), Black participants had significantly higher probability of cocaine use than White participants (B = 0.47, p<.001), participants recruited after 1988 had significantly higher probability of cocaine use than participants recruited in 1988 (B = 0.58, p<.001), and study visits in the 1990s (B = -.56, p<.001), 2000s (B = -1.12, p<.001), and 2010s (B = -1.58, p<.001) had successively lower rates of cocaine use than visits in the 1980s.

3.3.6 Sensitivity Analyses -- Participants Surviving to 2016

Results of the analysis repeated on the subsample of participants who survived until 2016 are shown in the Appendix Exhibits. As in the full sample, six-class models had the lowest AIC and BIC for both heroin and cocaine. Class structures were similar, but in general cessation classes tended to approach zero probability of use at younger ages.

3.4. Discussion

The analysis presented here offers new insight into the diverse possible courses of heroin and cocaine across the adult life of people with a history of injection drug use. While on average, the probability of continuing to use both drugs declines with age, this analysis suggests that this population-average decline may mask as many as six subtypes of users who experience a different course of disorder over the life course. Further, we find that these subtypes were actually quite similar for heroin and cocaine use. We did not model heroin and cocaine use in a joint model, mostly because of statistical constraints – due to the very long time period of observation with most cohort members observed for only part of the study period and because of the large number of classes explored, it was difficult to achieve convergence of the optimization algorithm used in model fitting. However, the similarity in class structure suggests that the trajectories observed are more a portrait of substance misuse behavior generally in people who inject drugs, rather than distinct trajectories of heroin and cocaine use respectively.

Specifically, for each drug: 1) We found three "cessation" groups – comprising around two-fifths of the sample for both heroin and cocaine use – that declined from higher than 50% probability of use to zero probability of use by participants mid 30s, 40s, or 50s, depending on group membership. 1) We found a "relapsing" group – comprised of a quarter of the cohort whether heroin or cocaine is the drug use outcome – who had a probability of use of just under 50% at every visit from age 30 to 60. 3) We found a "diminishing" group – collectively comprising about a quarter of the sample for both heroin and cocaine use – that also experienced declining probability of use with age, but that probability did not reach 0 by age 60. 4) Finally, about a tenth of the cohort for heroin use, and slightly less than that for cocaine use, experienced an accelerating pattern of use. These cohort members had achieved a low probability of use in mid-life, but this increased dramatically with age – in other words, this group experienced very high probability of relapse even after a long period of minimal use in midlife.

Taken together, aside from painting a novel portrait of the diverse courses that heroin and cocaine use can take over adult life, the subgroups described lend themselves to at least two practical conclusions. First, the course of heroin and cocaine use over adult life is more complex than previously described. Recall that Hser and colleagues (Hser et al., 2007) identified three latent trajectories of heroin use in a sample of about 500

participants, and Genberg and colleagues (Genberg et al., 2011) identified five latent trajectories of injection drug use in this same cohort, but with fewer study visits. We identified six latent trajectories, but did not test for seven or more class models, primarily because of sample size and interpretability constraints. It is reasonable to think that, if an even larger sample were available, more latent classes might be identified. In some respects, this is a limitation of the analysis – it strongly suggests that there are not "truly" some finite number of subgroups of people who use heroin or cocaine that could theoretically be identified with biological or behavior markers (or better modeling techniques). However, identifying more classes serves to illustrate the complexity of substance use disorders, and highlight less common, but still fairly prevalent, common trajectories of use.

Second, less than half of the sample – for both cocaine and heroin outcomes – fell in a cessation trajectory that achieved zero probability of use by age 60. The remainder had a non-trivial probability of heroin use even after age sixty. In fact, just under a tenth of the sample experienced accelerating trajectories with increasing risk for (heroin or cocaine) use late in life. This underscores the chronic nature of drug use behavior for these drugs, and also suggests that there is a not insignificant group who – even after an extended period with low to moderate drug use – will relapse to frequent in late life.

Recognizing this underlying heterogeneity that characterizes the course of heroin, cocaine, and speedball has implications for the present opioid epidemic. In particular, the findings presented here suggest that, though the current spike in overdose deaths is often treated as a short-term disaster or "crisis," in reality millions of Americans are struggling with chronic disorders, and many of these likely will continue to use opioid drugs like

heroin or co-use stimulants like cocaine for much of their adult lives; others who cease use may start again many years later. Efforts to identify these subgroups of high-risk users, and meeting the needs resulting from the impairment that likely accompanies this chronic use, will be an important complementary effort to emergency services to reduce overdose death rates.

Finally, we should note that we repeated our analysis among the sample of study participants who were still living in 2016. Surprisingly, while there were some differences, we found a generally similar class structure and similar class prevalences. In fact, it is worth noting that, even in this group of survivors, 11% of the sample demonstrated an "accelerating" trajectory for heroin use and 7% demonstrated an "accelerating" trajectory for cocaine use. More research is needed to understand the characteristics of this sub-population of adults who survive into older adulthood even as they relapse into very high probability of drug use.

The present analysis is descriptive, and is designed to motivate future research. The three conclusions noted, and their implications for the present opioid epidemic, strongly lend themselves to four follow-up areas of research:

- 1. What are the early-life characteristics that predict membership in one or another latent drug-use class for heroin or cocaine?
- 2. What are the factors that, over the course of life, modify the course of drug use, and do these factors vary by latent class membership? In other words, do different "types" of heroin and cocaine users have different sets of risk factors for persistent use or relapse?

- 3. How do heroin and cocaine use interact? How does use of one drug affect the onset or cessation of the other?
- 4. How is class membership, and the course of heroin or cocaine use more generally, associated with mortality?

These are all questions that can, and should, be answered through further analysis of the ALIVE cohort.

This study has a number of limitations. First, the cohort is comprised of Baltimorearea adults recruited in waves throughout the 1980s, 1990s, and 2000s. The strengths of this cohort for understanding long-term trajectories of drug use are that ALIVE is not a sample of people in treatment, and ALIVE has a very long period of follow-up. However, this mostly male, mostly African American, almost exclusively urban, east-coast cohort many of whom came of age during the peak of the HIV epidemic – are very different from the general population of drug users. In particular, there is an urgent need for research on rural substance use – trajectories of use may be very different in rural communities, where treatment availability is scarce (Jones, Campopiano, Baldwin, & McCance-Katz, 2015). Second, ALIVE participants are also unique in that they were recruited because they have a history of injecting drugs. Injection drug use may be a marker for severity of drug-related problems; different trajectories might be observed in the broader cohort of adults who use heroin or cocaine but have never injected. Third, latent variable methods can be unstable, and class structure and size estimates may differ when estimated in different populations. This limitation is particularly noteworthy in this study because of the first limitation – the geographic specificity of the ALIVE cohort. Fourth, the trajectories in this study relied on parametric assumptions, most importantly

1) a quadratic time trend and 2) a common probability of use across all classes at age 20. In the strictest sense, these assumptions are probably not accurate, and the former in particular is a limitation since participants were recruited at different ages, so it is difficult to know what their probability of drug use at 20 would have been. However, while more flexible model specifications are possible, they may come at the price of interpretability or, more practically, may simply not be estimable without a very large sample. The appropriate way to interpret the classes presented in this study are as an illustration of general trends, not as exact estimates of the probability of use at any particular age. Fifth, latent class linear mixed models assume each study participant is a member of exactly one, discrete class. In the strictest sense, this assumption is also not realistic in this study – it is implausible that there is a single biomarker like a gene that dictates the course of substance use disorder over the life course. Further, as a practical matter, the trajectories identified sometimes overlap in probability space, and their entropies are low (Table 2) (Celeux & Soromenho, 1996), suggesting poor class differentiation. It is more appropriate to view this analysis as a tool for identifying common trajectories of drug use, rather than of identifying truly distinct classes of users. Sixth, random intercept models are unbiased so long as study visits are "missing at random" (Bell, Kenward, Fairclough, & Horton, 2013), where "missing at random" refers to the concept defined by Rubin (Rubin, 1976). However, in addition to survival bias (addressed in our sensitivity analysis), study visits may be missing "not at random" if, during periods when participants did not attend visits, they were systematically more (or less) likely to be using heroin or cocaine. If this is the case, then estimated trajectories would be biased.

This study is the first to examine the heterogeneity of heroin, cocaine, and speedball use in a community population sample over an extended period of adult life. Findings suggest that the average declines in the probability of use over the course of life may mask distinct groups of high and low risk users. Future research is needed to better identify these groups, understand their needs, and reduce the proportion of drug users who continue to use throughout the course of adulthood.

3.6 References

- Ahrnsbrak, R., Bose, J., Hedden, S. L., Lipari, R. N., & Park-Lee, E. (2017). Key substance use and mental health indicators in the United States: Results from the 2016 National Survey on Drug Use and Health. *Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration: Rockville, MD, USA.*
- Associated Press. (2018, November 29). CDC says life expectancy down as more Americans die younger due to suicide and drug overdose. Retrieved December 6, 2018, from https://www.cbsnews.com/news/cdc-us-life-expectancy-decliningdue-largely-to-drug-overdose-and-suicides/
- Bell, M. L., Kenward, M. G., Fairclough, D. L., & Horton, N. J. (2013). Differential dropout and bias in randomised controlled trials: when it matters and when it may not. *The BMJ*, 346. https://doi.org/10.1136/bmj.e8668
- Celeux, G., & Soromenho, G. (1996). An entropy criterion for assessing the number of clusters in a mixture model. *Journal of Classification*, *13*(2), 195–212.
- Christie, G. C., Baker, C. G. C., Cooper, G. R., Kennedy, C. P. J., Madras, B., & Bondi,F. A. G. P. (n.d.). THE PRESIDENT'S COMMISSION ON COMBATINGDRUG ADDICTION AND THE OPIOID CRISIS.
- Genberg, B. L., Gange, S. J., Go, V. F., Celentano, D. D., Kirk, G. D., & Mehta, S. H.
 (2011). Trajectories of injection drug use over 20 years (1988–2008) in
 Baltimore, Maryland. *American Journal of Epidemiology*, 173(7), 829–836.
- Haastrup, S., & Jepsen, P. W. (1988). Eleven year follow-up of 300 young opioid addicts. *Acta Psychiatrica Scandinavica*, 77(1), 22–26.

- Healthcare Cost and Utilization Project (HCUP). (2018). HCUP Fast Stats. Rockville,
 MD: Agency for Healthcare Research and Quality. Retrieved from
 https://www.hcup-us.ahrq.gov/faststats/OpioidUseServlet
- Hser, Y.-I., Hoffman, V., Grella, C. E., & Anglin, M. D. (2001). A 33-Year Follow-up of Narcotics Addicts. *Archives of General Psychiatry*, 58(5), 503–508. https://doi.org/10.1001/archpsyc.58.5.503
- Hser, Y.-I., Huang, D., Chou, C.-P., & Anglin, M. D. (2007). Trajectories of heroin addiction: growth mixture modeling results based on a 33-year follow-up study. *Evaluation Review*, 31(6), 548–563. https://doi.org/10.1177/0193841X07307315
- Jones, C. M., Campopiano, M., Baldwin, G., & McCance-Katz, E. (2015, July 9). National and State Treatment Need and Capacity for Opioid Agonist Medication-Assisted Treatment [research-article]. https://doi.org/10.2105/AJPH.2015.302664
- Kolodny, A., Courtwright, D. T., Hwang, C. S., Kreiner, P., Eadie, J. L., Clark, T. W., & Alexander, G. C. (2015). The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. *Annual Review of Public Health*, 36, 559– 574.
- McCall Jones, C., Baldwin, G. T., & Compton, W. M. (2017). Recent Increases in Cocaine-Related Overdose Deaths and the Role of Opioids. *American Journal of Public Health*, 107(3), 430–432. https://doi.org/10.2105/AJPH.2016.303627

McLellan, A. T., Lewis, D. C., O'Brien, C. P., & Kleber, H. D. (2000). Drug
Dependence, a Chronic Medical Illness: Implications for Treatment, Insurance, and Outcomes Evaluation. *JAMA*, 284(13), 1689–1695.
https://doi.org/10.1001/jama.284.13.1689

- Murphy, S. L., Xu, J., Kochanek, K. D., & Arias, E. (n.d.). Mortality in the United States, 2017.
- National Institute on Drug Abuse. (2018, February 28). Florida Opioid Summary. Retrieved June 29, 2018, from https://www.drugabuse.gov/drugsabuse/opioids/opioid-summaries-by-state/florida-opioid-summary
- Patrick, S. W., Schumacher, R. E., Benneyworth, B. D., Krans, E. E., McAllister, J. M.,
 & Davis, M. M. (2012). Neonatal abstinence syndrome and associated health care expenditures: United States, 2000-2009. *Jama*, 307(18), 1934–1940.
- Price, R. K., Risk, N. K., & Spitznagel, E. L. (2001). Remission from drug abuse over a 25-year period: patterns of remission and treatment use. *American Journal of Public Health*, 91(7), 1107–1113.
- Proust-Lima, C., Philipps, V., & Liquet, B. (2015). Estimation of extended mixed models using latent classes and latent processes: the R package lcmm. *ArXiv Preprint ArXiv:1503.00890*.
- Robins, L. N., & Slobodyan, S. (2003). Post-Vietnam heroin use and injection by returning US veterans: clues to preventing injection today. *Addiction*, 98(8), 1053–1060. https://doi.org/10.1046/j.1360-0443.2003.00436.x
- Rubin, D. B. (1976). Inference and missing data. *Biometrika*, 63(3), 581–592.
- Saitz, R., Larson, M. J., LaBelle, C., Richardson, J., & Samet, J. H. (2008). The Case for Chronic Disease Management for Addiction. *Journal of Addiction Medicine*, 2(2), 55–65. https://doi.org/10.1097/ADM.0b013e318166af74

- Seth, P. (2018). Overdose Deaths Involving Opioids, Cocaine, and Psychostimulants United States, 2015–2016. MMWR. Morbidity and Mortality Weekly Report, 67. https://doi.org/10.15585/mmwr.mm6712a1
- Vlahov, D., Anthony, J. C., Munoz, A., Margolick, J., Nelson, K. E., Celentano, D. D., ... Polk, B. F. (1991). The ALIVE study, a longitudinal study of HIV-1 infection in intravenous drug users: description of methods and characteristics of participants. *NIDA Research Monograph*, (109), 75–100.
- Weiss, R. D., Potter, J. S., Fiellin, D. A., Byrne, M., Connery, H. S., Dickinson, W., ... Ling, W. (2011). Adjunctive counseling during brief and extended buprenorphinenaloxone treatment for prescription opioid dependence: a 2-phase randomized controlled trial. *Archives of General Psychiatry*, 68(12), 1238–1246. https://doi.org/10.1001/archgenpsychiatry.2011.121

Table 3.1. Prevalence of Drug Use, Characteristics, by Age Quartile at Visit					
	All	Q1: 19-38	Q2: 38-44	Q3: 44-51	Q4: 51-81
Number of Study Visits	56482	14128	14113	14129	14112
Heroin	46.6%	60.8%	54.5%	42.6%	28.4%
Cocaine	48.7%	63.6%	56.8%	44.3%	30.0%
Female	28.8%	32.1%	30.1%	28.7%	24.1%
Black	93.4%	91.1%	93.6%	94.1%	95.0%
Recruited After 1988	33.0%	23.8%	29.5%	37.7%	40.9%
1980s	5.3%	14.5%	4.8%	1.5%	0.3%
1990s	43.7%	69.8%	60.0%	34.7%	10.5%
2000s	30.6%	12.1%	28.3%	44.5%	37.4%
2010s	20.4%	3.6%	6.9%	19.3%	51.7%

3.7 Exhibits

Table 5.2. Fit Statistics for Latent Class Wodels with 2-0 Classes					
Number of Classes	2 Class	3 Class	4 Class	5 Class	6 Class
Heroin					
Log Likelihood	-25507.697	-25128.335	-24946.058	-24863.072	-24743.543
Entropy	0.41427156	0.51407239	0.42997516	0.42986008	0.44837635
AIC	51041.3948	50288.6695	49930.1167	49770.1433	49537.0863
BIC	51118.7879	50383.9226	50043.2298	49901.1163	49685.9192
Cocaine					
Log Likelihood	-24966.063	-24547.4	-24372.853	-24247.39	-24167.732
Entropy	0.40965059	0.45805936	0.43864151	0.46214933	0.50176624
AIC	49958.1268	49126.8001	48783.7057	48538.7802	48385.4641
BIC	50035.5199	49222.0532	48896.8188	48669.7532	48534.297

Table 3.2. Fit Statistics for Latent Class Models with 2-6 Classes

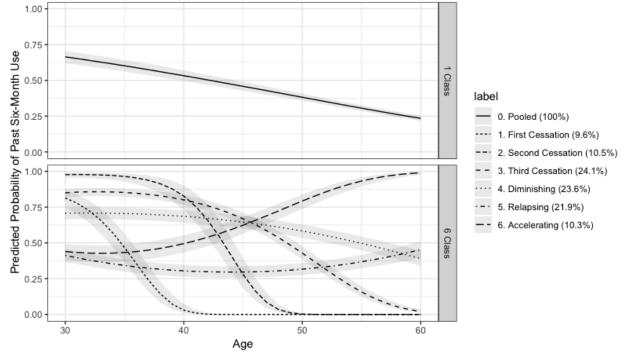


Figure 3.1. Single-Class (Pooled) and Six-Class Estimates of Predicted Probability of Heroin Use at Ages 30-60 in Baltimore Adults who Injected Drugs

Note: Predictions for hypothetical male, Black participant, recruited in a post-1988 wave, attending a study visit in the 2010s, and with a random intercept of 0.

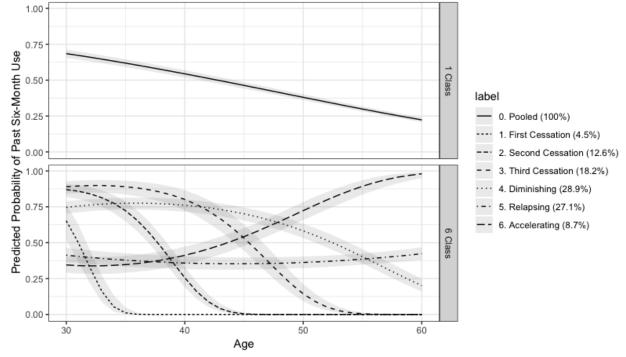


Figure 3.2. Single-Class (Pooled) and Six-Class Estimates of Predicted Probability of Cocaine Use at Ages 30-60 in Baltimore Adults who Injected Drugs

Note: Predictions for hypothetical male, Black participant, recruited in a post-1988 wave, attending a study visit in the 2010s, and with a random intercept of 0.

3.8 Appendix Exhibits

among rersons who Survived to 2010						
	All	Q1: 19-38	Q2: 38-44	Q3: 44-51	Q4: 51-81	
Number of Study						
Visits	33229	8309	8308	8307	8305	
Heroin	41.7%	60.1%	48.8%	34.7%	23.4%	
Cocaine	43.4%	59.5%	49.9%	37.4%	26.7%	
Female	30.8%	32.7%	33.5%	32.1%	24.8%	
Black	92.8%	87.9%	93.0%	94.3%	96.0%	
Recruited After 1988	43.4%	35.3%	43.2%	48.8%	46.3%	
1980s	2.9%	9.6%	1.8%	0.3%	0.0%	
1990s	32.1%	65.8%	44.4%	15.1%	2.9%	
2000s	34.3%	18.4%	40.7%	49.3%	28.6%	
2010s	30.7%	6.2%	13.1%	35.2%	68.5%	

Table 3.1a. Prevalence of Drug Use, Characteristics, by Age Quartile at Visit, among Persons who Survived to 2016

who Survived to 2010					
Number of Classes	2 Class	3 Class	4 Class	5 Class	6 Class
Heroin					
Log Likelihood	-14445.728	-14203.925	-14104.999	-14052.541	-13981.746
Entropy	0.48787741	0.50945642	0.47376305	0.46683488	0.49730096
AIC	28917.4555	28439.8501	28247.9973	28149.0815	28013.4918
BIC	28985.824	28523.996	28347.9205	28264.7821	28144.9697
Cocaine					
Log Likelihood	-14174.157	-13918.845	-13819.911	-13763.713	-13693.341
Entropy	0.51046892	0.52114598	0.48249954	0.47990204	0.52871646
AIC	28374.3142	27869.6891	27677.8214	27571.4252	27436.6823
BIC	28442.6827	27953.8349	27777.7446	27687.1257	27568.1602

Table 3.2a. Fit Statistics for Latent Class Models with 2-6 Classes, among Persons who Survived to 2016

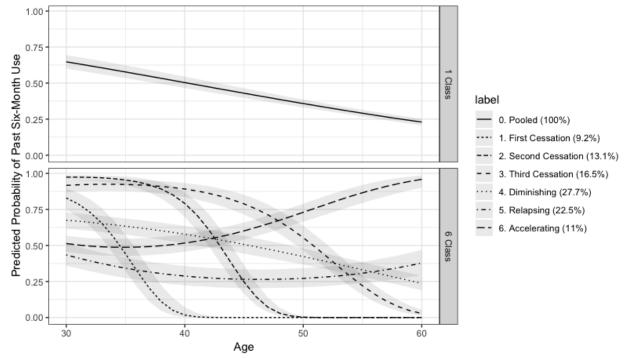


Figure 3.1a. Single-Class (Pooled) and Six-Class Estimates of Predicted Probability of Heroin Use at Ages 30-60 in Baltimore Adults who Injected Drugs and Survived to 2017

Note: Predictions for hypothetical male, Black participant, recruited in a post-1988 wave, attending a study visit in the 2010s, and with a random intercept of 0.

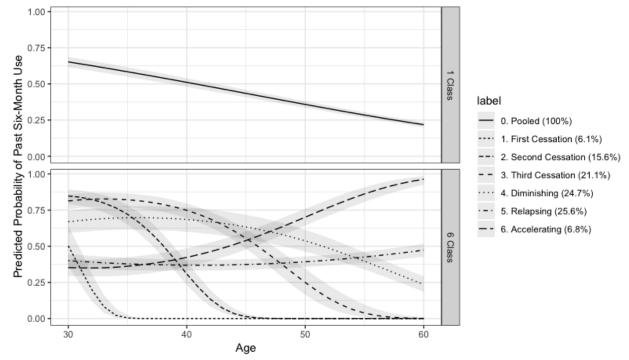


Figure 3.2a. Single-Class (Pooled) and Six-Class Estimates of Predicted Probability of Cocaine Use at Ages 30-60 in Baltimore Adults who Injected Drugs and Survived to 2017

Note: Predictions for hypothetical male, Black participant, recruited in a post-1988 wave, attending a study visit in the 2010s, and with a random intercept of 0.

CHAPTER 4. ASSOCIATION OF CHILDHOOD ADVERSITY WITH HEROIN AND COCAINE USE ACROSS THE LIFE COURSE OF PEOPLE WHO INJECT DRUGS

4.0 Abstract

Background: Childhood adversity is associated with the development of substance use problems in adulthood, including opioid and cocaine misuse. To my knowledge, no research has examined how a history of childhood adversity modifies the course of substance use over an extended period of adult life.

Methods: Data were collected as part of ALIVE, a longitudinal cohort under observation since 1988 with community-based recruitment of adults who currently inject or formerly injected drugs from the Baltimore area. Past six-month heroin and cocaine use by any route of administration were assessed at twice-annual study visits conducted between 1988 and 2016. In 2018, childhood adversity was retrospectively assessed in 352 participants via self-report interview by a trained clinician. Bayesian multilevel models were used to test the hypothesis that childhood adversity modifies the association of age with substance use.

Results: For participants with fewer than two adverse childhood experiences, the probability of both heroin and cocaine use declined sharply with age, to less than 10 percent for both heroin and cocaine by age 65. By contrast, risk for heroin and cocaine use persisted into older ages among participants with 5 or more adverse childhood experiences, remaining above 40% for both heroin and cocaine use.

Conclusion: Among people who have injected drugs, a history of childhood adversity is associated with a substantially increased probability of continuing to use heroin and cocaine at older ages. More research is needed to understand why the negative effects of childhood adversity on drug use behavior persist, and indeed grow stronger, at older ages.

4.1 Introduction

As discussed in the previous chapters, the United States is experiencing an unprecedented epidemic of drug-related problems. Most research on the causes of the United States' ongoing epidemic has focused on proximal events that have increased deaths from opioids, most notably: 1) over-prescribing of opioid pain-relievers like OxyContin over the past three decades (Kolodny et al., 2015); 2) growing use of highly potent and lethal fentanyl (Miller, Stogner, Miller, & Blough, 2017; National Institute on Drug Abuse, 2018); and 3) increasing deaths from stimulant drugs like cocaine, often when used in conjunction with opioids (Miller et al., 2017; Seth, 2018).

By contrast, the role of early-life risk factors that may influence the initiation and course of harmful opioid use has received comparatively little focus in the present epidemic. The omission of early-life risks from research and policy efforts likely reflects a desire to study proximal targets that may be useful for preventing overdose deaths and ameliorating the present crisis. However, there are reasons to believe a better understanding of the role of childhood risk factors in the present crisis – in particular, chronic childhood adversity and trauma – can play an important role in better addressing that crisis. This is because of the strong evidence that exposure to childhood adversity such as abuse, household dysfunction, or community violence are important precursors to opioid use disorder.

As discussed in greater detail in the Introductory Chapter, there is strong evidence that exposure to abuse, household dysfunction, or other forms of adversity in childhood are associated with observable structural and functional changes in adult brain regions and systems linked to addiction (Enoch, 2011). Further, this adversity is associated with

increased risk for use of "street drugs," earlier initiation of drug use, self-identified addiction to drugs (Dube et al., 2003), injection drug use (Ompad et al., 2005) and alcohol use disorder (Anda et al., 2006). In fact, childhood adversity is also related to a host of mental, behavioral, and physical problems linked to substance use, including many of the leading causes of death (Anda et al., 2006; Felitti et al., 1998). Childhood trauma has even been identified as a risk factor for an opioid use disorder specifically (Naqavi, Mohammadi, Salari, & Nakhaee, 2011), and some authors have argued that a history of childhood trauma plays a central role in the etiology of heroin use disorder (Darke, 2013). Childhood abuse and household dysfunction are also associated with increased risk for two of the primary drivers of the present opioid epidemic – chronic pain (Davis, Luecken, & Zautra, 2005) and use of a greater number of prescription medications (Anda, Brown, Felitti, Dube, & Giles, 2008).

In summary, there is a clear and strong link between childhood adversity and both adult substance use generally and opioid-related problems specifically. However, knowing that adversity increases risk for developing opioid-related problems is, while useful, insufficient for meeting the needs of the more than 2 million Americans who are already living with opioid use disorder (Ahrnsbrak, Bose, Hedden, Lipari, & Park-Lee, 2017). To maximize prevention and intervention efforts, it is also vital to understand how childhood adversity affects the course of problem opioid use over the adult life span. If childhood adversity is differentially associated with greater probability or severity of drug related problems at different points in the life course, then this information can inform the development of interventions that explicitly address the known biological and psychosocial consequences of past adversity. By contrast, if childhood adversity is a risk

factor for the onset of drug problems, but does not influence the course of these problems, then trauma-oriented research and interventions designed to address trauma sequelae may have less utility for addressing the current opioid crisis, even if they help clients in other ways (e.g., by managing negative symptoms associated with trauma).

This study examines the effect of exposure to childhood adversity on the course of heroin and cocaine use over an extended period of adulthood. It uses data from the same AIDS Linked to the Intravenous Experience (ALIVE) study described in Chapter 3. In Chapter 3, we showed that average gradual declines in heroin and cocaine use with age may mask substantial heterogeneity in the population, with some participants relapsing to very high probability of use in late adulthood even after a period of extended abstinence. In this chapter, we examine if childhood adversity modifies the trajectory of heroin and cocaine use over the life course, thereby explaining some of this heterogeneity. We hypothesize that childhood adversity is associated with higher probability of heroin and cocaine use in early adulthood, but that these effects will dissipate as participants age and childhood experiences become more distant.

4.2 Materials and Methods

4.2.1 Study Participants

Study participants were recruited into the ALIVE study, an active, communitybased, prospective cohort study of adults living in and around Baltimore City, Maryland who have injected drugs and who agree to attend twice annual study visits. Details of that study are described in Chapter 3.

The present analysis used data from 362 ALIVE participants who completed a retrospective assessment of adverse childhood experiences between August 1st and

December 26th of 2018. Of these, 10 participants were excluded because they declined to complete the section of the assessment examining child abuse (see below), for a final sample of 352 participants. These 352 participants collectively attended 8,231study visits at various points between 1988 and 2017. Of these visits, 218 were excluded because data on participants past six-month heroin or cocaine use were missing (see 2.2. Measures), leaving a final sample of 8,013 visits used in this analysis.

(More than 362 ALIVE participants attended study visits during that time period, but did not complete the adverse childhood experiences assessment, primarily because of constraints on staff time. We did not track these participants, because data collection is ongoing, and we intend to offer them the opportunity to complete the questionnaire at their next visit.)

The Johns Hopkins University institutional review board approved the ALIVE study, and data collection for this sub-study. All participants provided informed written consent to participate. In addition, six questions included in our assessment asked participants about childhood experiences that likely constitute child abuse. Maryland State law requires that incidents of child abuse uncovered in the context of research be reported by the researchers to the city Department of Social services. For this reason, prior to asking participants' these six questions, participants were told:

"In the next section, I'm going to ask some more questions about some things that an adult might have said or done to you <u>before your 18th birthday</u>. Some of these things could indicate that, when you were a child, you experienced abuse. For this reason, if you answer yes to any of these next six questions, under Maryland State law, I will be obligated to make a report including your name and contact

information to the Baltimore City Department of Social Services.... Would you like me to proceed with this section?"

If participants chose to proceed, and endorsed any of the subsequent items, a report was made to the Baltimore Department of Social Services, as required by Maryland law. Only 10 of 362 participants (3%) declined to complete this section after hearing this statement (see above).

4.2.2 Measures

4.2.2.1 Outcome. Two outcomes were assessed in this analysis: 1) Past six-month heroin use by any route of administration assessed in ALIVE (injecting heroin alone, snorting heroin alone, smoking heroin alone, and injecting heroin and cocaine simultaneously). 2) Past six-month cocaine use by any route of administration assessed in ALIVE (injecting cocaine alone, snorting cocaine, smoking crack cocaine, and injecting heroin and cocaine simultaneously). All outcomes were assessed at each study visit via self-report in response to audio-computer-assisted-survey instruments (ACASI).

4.2.2.2 Exposure. The primary independent variable was a participant's age in days at a study visit.

4.2.2.3 Effect Modifier. Participants' childhood exposure to adversity and trauma was assessed using a modified version of the Adverse Childhood Experiences questionnaire (Finkelhor, Shattuck, Turner, & Hamby, 2015). This assessment is based on the classic assessment administered by Felitti and colleagues to members of the Kaiser health system for the CDC's Adverse Childhood Experience Study (Felitti et al., 1998), but adds four other common adverse experiences shown to predict poor outcomes

(Finkelhor et al., 2015). Assessments were administered as part of an in-person interview by trained clinicians (a nurse and nurse-practitioner).

Fourteen adverse childhood experiences were assessed, with 21 questions: physical neglect (2 questions), emotional neglect (2 questions), physical abuse (2 questions), emotional abuse (2 questions), sexual abuse (2 questions), loss of a parent to divorce, abandonment or "some other reason" (1 question), growing up with domestic violence in the home (3 questions), having a parent with an alcohol or drug use problem (1 question), having a parent with mental illness (1 question), having a member of the household go to prison (1 question), being bullied by peers (1 question), being ostracized by peers (1 question), growing up in a violent neighborhood (1 question), and growing up in poverty (1 question). For adversities assessed with multiple items, endorsing any one of those items was sufficient to indicate the presence of that adversity. The 14 dichotomized items were summed to compute a scale score ranging from 0 to 14. This scale was further grouped into tertiles of 0-1 adversities, 2-4 adversities, and 5 or more adversities for analytic purposes. Tertiles were used instead of the commonly used grouping of 0, 1, 2, 3, or 4 or more adversities for two reasons: first, a smaller number of groups was needed to make age-by-adversity interaction terms estimable (see 2.3 Analytic Approach); second, because exploratory analysis showed very high levels of adversity were reported in the cohort, we wanted childhood adversity groupings that appropriately reflect the distribution of adversity in this sample.

4.2.2.4 Potential Confounders. We adjusted for the demographic variables gender (male, female) and race (Black, White) and for study-specific variables 'decade of

study visit' (1980s, 1990s, 2000s, 2010s) and 'recruitment cohort' (initial 1988 recruitment, or all other cohorts).

4.2.3 Analytic Approach

4.2.3.1 Summary. The analytic approach is the same for both outcome drugs (heroin and cocaine), so going forward we refer generally to the outcome as "drug use." The goal of the analysis was to determine how a history of childhood adversity modifies the probability of drug use over the adult life course. We examined this question by using Bayesian multi-level logistic regression models to estimate the conditional probability of drug use as a function of age. We included an interaction term to determine whether a history of childhood adversity modified the association of age with drug use. We then estimated the relative odds of drug use comparing participants who experienced high levels of adversity to participants who experienced low levels of adversity, in years of life between age 30 and 65 (95% of study visits fell in this age range).

4.2.3.2 Missing Questionnaire Responses. All 352 participants whose data informed analyses answered at least one item on the childhood adversity assessment; however, 44 (12.5%) left at least one of these items unanswered. Exploratory analysis showed the 44 participants who failed to respond to at least one adversity question were more likely to endorse other adversities. To maximize our sample size and avoid inducing selection bias, before conducting the analysis, we multiply-imputed missing responses using participants' responses to other questionnaire items with conditional mean matching. Five imputed datasets were created. Participants' childhood adversity score was computed in each of the five imputed datasets (see 2.2.3 Effect Modifier). The

subsequent analysis was conducted on each dataset, and results were pooled across sets (see 2.3.4 Model Estimation).

4.2.3.3 Analytic Model. The conditional probability of drug use as a function of age was estimated using Bayesian multi-level logistic regression models. Age was modeled using a 3-degree natural cubic spline with knots at 44 and 53 years to separate age tertiles. Models were adjusted for all confounders. Participant-specific intercepts (also known as random intercepts) were included, to account for the correlation between responses from the same participant.

To assess the effect of childhood adversity, the model above was extended by including an interaction term between each age spline term and each childhood adversity tertile. The fit of models with and without interaction effects were compared using WAIC (Vehtari, Gelman, & Gabry, 2017), to ensure inclusion of the interaction term improved expected out-of-sample predictive accuracy.

Bayesian models require specification of a prior distribution for parameters. We used non-informative priors: improper flat priors for all regression coefficients; a tdistribution with mean 0, variance 10, and three degrees of freedom for the grand mean of the participant-specific intercept; and a half-t-distribution with mean 0, variance 10, and three degrees of freedom for the variance of the participant-specific intercept. These are the defaults for the modeling software used and are consistent with our lack of prior knowledge about model parameters given the novelty of this study.

4.2.4.4 Model Estimation. Posterior distributions for all model parameters were estimated with Markov Chain Monte Carlo (MCMC) simulation using the modified Hamiltonian Monte Carlo "No U-Turn Sampler" (Hoffman & Gelman, 2014). In each of

the five imputed datasets, two Markov chains with different starting values were executed, for a total of 10 chains. Each chain contained 1,000 samples, half of which were thrown away as a "warm-up" period. For each parameter, chains were compared using the R-hat scale reduction statistic to assess model convergence (Stan Development Team, 2018). Chains were then pooled into 5,000 MCMC draws that were used to summarize the posterior distribution.

4.2.4.5 Model Interpretation and Inference. Because age is modeled using natural cubic splines, it is impossible to interpret model coefficients directly. Instead, post-hoc calculations are required to answer the scientific question of interest. By transforming linear combinations of coefficients, we calculated:

- The predicted probability of drug use at each year of age for each level of childhood adversity, for a male Black participant (the most common demographic), recruited in a post-1988 cohort and attending a study visit in 2010 (to make estimates more representative of present day) and a random intercept of 0.
- 2. The relative odds of drug use at each age comparing a participant with high childhood aversity (5 or more adversities) to a participant with low childhood adversity (1 or 0 adversities).

This calculation was conducted for each of the 5,000 MCMC draws to produce a full posterior distribution for all predicted probabilities and odds ratios. To summarize these distributions, we use the posterior median as a point estimate and the 0.025 and 0.975 quantiles as bounds of a 95% Bayesian credible interval – in other words, there is a 95% chance the probability/odds ratio falls in that interval.

4.2.4.6 Software. All analyses were conducted in R version 3.4.3 (R Core Team, 2017). Multiple imputation was conducted using the 'mice' package (van Buuren & Groothuis-Oudshoorn, 2011). Bayesian models were estimated using the 'brms' package (Buerkner, 2016), which relies on Stan, a language for Bayesian modeling with Hamiltonian Monte Carlo sampling (Carpenter et al., 2017).

4.3. Results

4.3.1 Demographics and Childhood Adversity

Of 352 participants, 69% were male, 82% were Black, and 73% joined the ALIVE cohort after the initial 1988 recruitment.

The mean number of adverse childhood experiences reported was 4, and 80% of the sample reported at least 1 of the 14 adverse experiences. The most common adversity was growing up in a violent neighborhood (52.3%) followed by growing up in poverty (41.2%), and the loss of a parent (37.7%).

4.3.2 Drug Use.

4.3.2.1 Heroin. Heroin use was reported at 40% of all study visits. Heroin use was reported at 39% of all study visits from participants who reported 0 or 1 adverse childhood experience, 38% of study visits from participants who reported 2 to 4 adverse experiences, and 43% of study visits from participants who reported five or more adverse experiences.

4.3.2.2 Cocaine. Cocaine was reported at 45% of study visits. Cocaine use was reported at 43% of study visits from participants who experienced 0 or 1 adverse childhood experience, 42% of visits from participants who experienced 2 to 4 adverse

experiences, and 48% of visits from participants who reported 5 or more adverse experiences.

4.3.3 Effect of Childhood Adversity

4.3.3.1 Heroin. In a model not accounting for childhood adversity, the predicted probability of heroin use declined from 80.5% (95% CI 69.8% to 88.1%) at age 35 to 61% (95% CI 49.6% to 71.9%) at age 45, 33.0% (95% CI 23.9% to 42.6%) at age 55, and 16.9% (95% CI 10.4% to 26.0%) at age 65. Adding terms for the interactions of age spline with childhood adversity improved model predictive accuracy (Null WAIC = 6,671; Extended WAIC = 6,589). There were essentially no differences between the 0-to-1 adversity group and the 2-to-4 adversities group. When comparing the 5-or-more adversity group to the 0-to-1 adversity group, the odds of heroin use were lower in the 5-or-more group at age 35 (OR 0.39, 95% CI 0.17 to 0.88); this gap narrowed quickly and reversed, so that by age 65 heroin use was much more likely in the 5-or-more group (OR 10.71, 95% CI 3.81 to 32.8).

4.3.3.2 Cocaine. In a model not accounting for childhood adversity, the predicted probability of cocaine use declined from 80.9% (95% CI 70.0% to 88.3%) at age 35 to 64.5% (95% CI 53.3% to 74.3%) at age 45, 32.2% (95% CI 23.9% to 42.2%) at age 55, and 14.4% (95% CI 8.9% to 22.5%) at age 65. Adding terms for the interactions of age spline with childhood adversity improved model predictive accuracy (Null WAIC = 6676; Extended WAIC = 6639). There were essentially no differences in between the 0 to 1 adversity group and the 2 to 4 adversities group. When comparing the 5-or-more adversity group to the 0-to-1 adversity group, the odds of cocaine use were lower in the 5-or-more group at age 35 (OR 0.69, 95% CI 0.31 to 1.53); this gap narrowed quickly

and reversed, so that by age 65, cocaine use was much more likely in the 5-or-more group (OR 15.57, 95% CI 5.15 to 45.92).

4.4 Discussion

As expected, childhood adversity was very common among Baltimore city adults with a history of drug use. Eight out of ten study participants reported at least once adverse experience. By contrast only four out of ten members of a representative sample of the Maryland adults who participated in the 2015 Behavioral Health Risk Factor Surveillance System (BRFSS) survey reported at least one adverse experience (Maryland Behavioral Risk Factor Surveillance System, 2017). This wide gap in part reflects that our study questionnaire assessed for four additional types of adversity, including childhood poverty, bullying, social isolation, and neighborhood violence that were not included in the Maryland questionnaire, and that were among the most frequently reported by ALIVE participants. However, even if those four items are excluded, seven out of ten ALIVE participants report at least one adversity. These descriptive results are consistent with a robust literature finding that a history of adversity and trauma are common among adults who use drugs (Hughes et al., 2017).

Further, these results offer new evidence that past experiences of childhood adversity have a lasting impact on the course of heroin and cocaine use for people who have injected drugs. Indeed, these effects last decades into adulthood. These findings are novel. Other studies, noted in the Introduction, focused on the association of childhood adversity with snapshots of drug use at a single point in time. Therefore, past research could indicate that adversity either increases risk for the onset of substance use problems, or that childhood adversity increases the duration and severity of substance use problems.

By following the use behaviors of a cohort of people who have all used drugs over a period of 30 years, this study is to my knowledge the first to show that, even among people who are already using heroin and cocaine, childhood adversity continues to modify the course of use over many years of life.

Moreover, we found that, among people recruited for a study based on their past injection drug use, childhood adversity was primarily associated with elevated risk for heroin and cocaine use later in life. When participants were in their thirties, the probability of heroin and cocaine use was very high across all groups. However, over time, this risk declined sharply for adults who experienced fewer than 5 childhood adversities. By contrast, for adults who experienced five or more childhood adversities, risk for both heroin and cocaine use never declined much below 50 percent even as participants reached their late 50s and early 60s. This suggests that a history of substantial childhood adversity is an impediment to recovery.

Notably, this delayed effect of childhood adversity is the opposite of our hypothesis that the effects of adversity would erode over time. Understanding why the effects of childhood experiences intensify over time is an essential question for future research. While we can only speculate, several hypotheses seem worthy of examination:

One possibility is that childhood abuse and trauma result in the development of maladaptive attachment styles that impede the formation and maintenance of healthy interpersonal relationships in adulthood (McCarthy & Taylor, 1999). Peer support has long been a part of the path to recovery from substance use problems (Tracy & Wallace, 2016). Further, multiple studies have found that maladaptive attachment styles are common in people with substance use problems, and are associated with greater

psychopathology in that population (Diaz, Horton, & Malloy, 2014; Rick, Vanheule, & Verhaeghe, 2009; Thorberg & Lyvers, 2006). In addition, animal studies and brainimaging studies have indicated a role for mu-opioid receptors in the biology insecure attachment, and those same systems play an important role in the biology of addiction as well (Nummenmaa et al., 2015; Renk et al., 2015). Taken together, these studies suggest a mechanism whereby the childhood adversity impairs the formation of trusting and supportive informal relationships needed to facilitate recovery, or possibly impede formation of more formal relationships in the context of treatment.

A second possibility is that, as noted, a history of child abuse is linked to a wide range of physical health problems (Anda et al., 2006), and in particular to chronic pain (Davis et al., 2005). It may be that, for people who have a history of high childhood adversity, heroin or cocaine use are means of compensating for these health problems and associated pain; so long as these related physical health problems remain, use continues and recovery is impeded.

A third possibility is that very high levels of childhood adversity might cause other negative outcomes that inadvertently protect against substance use. For example, a history of childhood adversity is associated with adolescent and adult criminal behavior (Baglivio et al., 2014; Reavis, Looman, Franco, & Rojas, 2013). If participants experiencing the highest levels of adversity are regularly in and out of jail, this could reduce heroin or cocaine use in the six months prior to an ALIVE study visit simply because a substantial portion of time is spent incarcerated. Since criminal behavior declines dramatically as adulthood advances (Ulmer & Steffensmeier, 2014), effects of

childhood adversity on drug use in a cohort where drug use is common may only emerge in older age.

Finally, a fourth possibility is that exposure to childhood adversity and adult drug use share common genetic risk. While seemingly counterintuitive, there is actually substantial evidence that genes influence children's exposure to maladaptive parenting behaviors – this happens because genetically influenced characteristics like appearance, temperament, and impulse control in turn influence how parents and other adults treat children (Baglivio et al., 2014; Reavis, Looman, Franco, & Rojas, 2013). It may be the study participants who have the highest genetic predisposition for impulsivity or antisocial behavior were both at high risk for exposure to childhood adversity and high risk for adult heroin and cocaine use because of these genes.

These explanations are neither exhaustive nor mutually exclusive. However, regardless of the cause, the findings of this study have important implications for the treatment of heroin and cocaine use disorders. Specifically, they suggest that high levels of childhood trauma may play an increasingly important role in unremitting or relapsing cases of substance use disorder. To meet the needs of these most challenging clients, it will be important to develop, adopt, and evaluate programs that address the lasting psychological, behavioral, and physical impacts of childhood adversity and trauma. Indeed, the existing body of adverse childhood experiences research has launched a growing movement to try to promote "trauma-informed practice" within healthcare and other social service settings (Ko et al., 2008; Muskett, 2014). Indeed, the Substance Abuse and Mental Health Administration (SAMHSA) identifies six principles that trauma informed care should address: safety; trustworthiness and transparency; peer support;

collaboration and mutuality; empowerment; voice and choice; and cultural, historical, and gender issues (National Center for Trauma-Informed Care and Alternatives to Seclusion and Restraint, 2018). However, there is widespread confusion about how to incorporate these principles into behavioral health practice, and few studies examining whether "trauma-informed" programs offer superior care (Muskett, 2014). This is an important area for future research. In the meantime, given the urgency of the present opioid crisis, the results of this study suggest that testing and adoption of trauma-informed practice in substance use treatment is a worthy and urgent public health goal.

Finally, two unusual findings should be noted. First, unlike Felitti and colleagues (Felitti et al., 1998), we did not observe a dose-response relationship between adversity and health – instead, low- and moderate adversity groups exhibited comparable probabilities of heroin and cocaine use over the life course, with only the high-adversity group diverging. Second, we found that, in early adulthood, a history of adversity appeared to protect against heroin use. We suspect the latter finding is spurious, since no similar association was seen for cocaine use. However, another possibility, noted above, is that very high levels of childhood adversity also increase risk for the competing outcome like incarceration or institutionalization, which could prevent drug use at least temporarily. As for the former, more research is needed to understand if there is either a threshold effect of adversity, if it is only the presence of particular adverse experiences that lead to sustained heroin and cocaine use, or we simply had insufficient power to detect the smaller effect of fewer adversities.

This study has a number of limitations. 1) The sample size – 352 participants contributing 8,013 visits – is small, especially considering the inclusion of interaction

effects and the need to use a flexible function to model the effects of age. Data collection is ongoing, and we intend to repeat this analysis with a larger sample, to solidify conclusions and reduce estimation uncertainty. 2) The study focuses on only two drugs – heroin and cocaine. Unfortunately, other opioid drugs such as prescription pain-relievers and fentanyl were not assessed for much of the observation period. Our necessary focus on heroin and cocaine limits the extent findings can be generalized to adults struggling with the current opioid epidemic. However, data collection about other opioid drugs is also now ongoing, and may be a focus of future analyses. Future research should also examine use of legal but dangerous substances like alcohol and tobacco. 3) This mostly male, mostly African American, almost exclusively urban, east-coast cohort - many of whom came of age during the peak of the HIV epidemic – are very different from the general population of drug users. In particular, there is an urgent need for research on rural substance use – the effects of adversity on use may be very different in rural communities, where treatment availability is scarce (Jones, Campopiano, Baldwin, & McCance-Katz, 2015). 4) ALIVE participants are also unique in that they were recruited because they had a history of injecting drugs. Injection drug use may be a marker for severity of drug-related problems; different effects of adversity might be observed in the broader cohort of adults who use heroin or cocaine but have never injected. 5) Childhood adversity was assessed retrospectively. If active drug use is differentially associated with differential recall of childhood experiences, then results could be biased. 6) Sixth, the childhood adversity questionnaire used is not the most widely used version assessment, and not the one used in the Maryland BRFSS. We chose this questionnaire because were seeking comparability with another large Baltimore cohort study, but that study

ultimately decided not to assess childhood adversity after our data collection had already begun. Unfortunately, we are therefore limited in our ability to compare study results to other populations. 6) Sixth, random intercept models are unbiased if study visits excluded for missing data are either "missing completely at random" or "at random," but not if visits are missing "not at random." (Rubin, 1976). If, for example, participants were more likely to miss study visits or not report information at times when they were also more likely to be using heroin or cocaine, then estimates would be biased. 7) Finally, the requirement that we report items indicating a history of child abuse to the department of social services – and the need to notify participants of that requirement – may have led to an undercount of the number of participants who actually experienced childhood abuse.

4.5 Conclusion

This study is, to our knowledge, the first to examine the effects of childhood adversity on risk for heroin and cocaine use over an extended period of life in a population where illicit substance use is endemic. We show that the effects of high adverse childhood experience persist into late adulthood, and impede cessation of heroin and cocaine use. Future research is warranted to examine the biological and psychological mechanisms behind these long-lasting effects. Further, these findings suggest that past traumatic experiences are an important target for substance use treatment programs, and that explicitly attempting to address the immediate and longterm consequences of trauma may help facilitate recovery for some of the most persistent users of heroin and cocaine.

4.6 References

- Ahrnsbrak, R., Bose, J., Hedden, S. L., Lipari, R. N., & Park-Lee, E. (2017). Key substance use and mental health indicators in the United States: Results from the 2016 National Survey on Drug Use and Health. *Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration: Rockville, MD, USA.*
- Anda, R. F., Brown, D. W., Felitti, V. J., Dube, S. R., & Giles, W. H. (2008). Adverse childhood experiences and prescription drug use in a cohort study of adult HMO patients. *BMC Public Health*, 8(1), 198.
- Anda, R. F., Felitti, V. J., Bremner, J. D., Walker, J. D., Whitfield, C. H., Perry, B. D., ... Giles, W. H. (2006). The enduring effects of abuse and related adverse experiences in childhood. *European Archives of Psychiatry and Clinical Neuroscience*, 256(3), 174–186.
- Avinun, R., & Knafo, A. (2014). Parenting as a reaction evoked by children's genotype:
 A meta-analysis of children-as-twins studies. *Personality and Social Psychology Review*, 18(1), 87–102.
- Baglivio, M. T., Epps, N., Swartz, K., Huq, M. S., Sheer, A., & Hardt, N. S. (2014). The prevalence of adverse childhood experiences (ACE) in the lives of juvenile offenders. *Journal of Juvenile Justice*, 3(2).
- Buerkner, P.-C. (2016). brms: An R package for Bayesian multilevel models using Stan. Journal of Statistical Software.

- Carpenter, B., Gelman, A., Hoffman, M. D., Lee, D., Goodrich, B., Betancourt, M., ... Riddell, A. (2017). Stan: A probabilistic programming language. *Journal of Statistical Software*, 76(1).
- Darke, S. (2013). Pathways to heroin dependence: time to re-appraise self-medication. *Addiction*, *108*(4), 659–667.
- Davis, D. A., Luecken, L. J., & Zautra, A. J. (2005). Are reports of childhood abuse related to the experience of chronic pain in adulthood?: a meta-analytic review of the literature. *The Clinical Journal of Pain*, 21(5), 398–405.
- Diaz, N., Horton, E. G., & Malloy, T. (2014). Attachment Style, Spirituality, and Depressive Symptoms Among Individuals in Substance Abuse Treatment. *Journal of Social Service Research*, 40(3), 313–324. https://doi.org/10.1080/01488376.2014.896851
- Dube, S. R., Felitti, V. J., Dong, M., Chapman, D. P., Giles, W. H., & Anda, R. F. (2003). Childhood abuse, neglect, and household dysfunction and the risk of illicit drug use: the adverse childhood experiences study. *Pediatrics*, *111*(3), 564–572.
- Enoch, M.-A. (2011). The role of early life stress as a predictor for alcohol and drug dependence. *Psychopharmacology*, *214*(1), 17–31.
- Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V.,
 ... Marks, J. S. (1998). Relationship of childhood abuse and household
 dysfunction to many of the leading causes of death in adults: The Adverse
 Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine*,
 14(4), 245–258.

- Finkelhor, D., Shattuck, A., Turner, H., & Hamby, S. (2015). A revised inventory of adverse childhood experiences. *Child Abuse & Neglect*, 48, 13–21.
- Hoffman, M. D., & Gelman, A. (2014). The No-U-turn sampler: adaptively setting path lengths in Hamiltonian Monte Carlo. *Journal of Machine Learning Research*, 15(1), 1593–1623.
- Hughes, K., Bellis, M. A., Hardcastle, K. A., Sethi, D., Butchart, A., Mikton, C., ...
 Dunne, M. P. (2017). The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. *The Lancet Public Health*, 2(8), e356–e366.
- Jones, C. M., Campopiano, M., Baldwin, G., & McCance-Katz, E. (2015, July 9). National and State Treatment Need and Capacity for Opioid Agonist Medication-Assisted Treatment [research-article]. https://doi.org/10.2105/AJPH.2015.302664
- Kiff, C. J., Lengua, L. J., & Zalewski, M. (2011). Nature and Nurturing: Parenting in the Context of Child Temperament. *Clinical Child and Family Psychology Review*, 14(3), 251–301. https://doi.org/10.1007/s10567-011-0093-4
- Ko, S. J., Ford, J. D., Kassam-Adams, N., Berkowitz, S. J., Wilson, C., Wong, M., ...
 Layne, C. M. (2008). Creating trauma-informed systems: Child welfare,
 education, first responders, health care, juvenile justice. *Professional Psychology: Research and Practice*, *39*(4), 396–404. https://doi.org/10.1037/07357028.39.4.396
- Kolodny, A., Courtwright, D. T., Hwang, C. S., Kreiner, P., Eadie, J. L., Clark, T. W., & Alexander, G. C. (2015). The prescription opioid and heroin crisis: a public health

approach to an epidemic of addiction. *Annual Review of Public Health*, *36*, 559–574.

Maryland Behavioral Risk Factor Surveillance System. (2017). Adverse Childhood
Experiences (ACEs) in Maryland: Data from the 2015 Maryland BRFSS.
Statewide and county-level estimates for non-institutionalized Maryland adults
age 18+. Retrieved from
https://phpa.health.maryland.gov/ccdpc/Reports/Documents/MD-

BRFSS/2015_MD_BRFSS_ACEs_Data_Tables.pdf

- McCarthy, G., & Taylor, A. (1999). Avoidant/Ambivalent Attachment Style as a Mediator between Abusive Childhood Experiences and Adult Relationship Difficulties. *The Journal of Child Psychology and Psychiatry and Allied Disciplines*, 40(3), 465–477.
- Miller, J. M., Stogner, J. M., Miller, B. L., & Blough, S. (2017). Exploring synthetic heroin: Accounts of acetyl fentanyl use from a sample of dually diagnosed drug offenders. *Drug and Alcohol Review*.
- Muskett, C. (2014). Trauma-informed care in inpatient mental health settings: A review of the literature. *International Journal of Mental Health Nursing*, *23*(1), 51–59. https://doi.org/10.1111/inm.12012
- Naqavi, M. R., Mohammadi, M., Salari, V., & Nakhaee, N. (2011). The relationship between childhood maltreatment and opiate dependency in adolescence and middle age. *Addiction & Health*, *3*(3–4), 92.
- National Center for Trauma-Informed Care and Alternatives to Seclusion and Restraint. (2018). *Trauma-Informed Approach and Trauma-Specific Interventions*.

Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/nctic/trauma-interventions

- National Institute on Drug Abuse. (2018, August 9). Overdose Death Rates. Retrieved December 6, 2018, from https://www.drugabuse.gov/related-topics/trendsstatistics/overdose-death-rates
- Nummenmaa, L., Manninen, S., Tuominen, L., Hirvonen, J., Kalliokoski, K. K., Nuutila, P., ... Sams, M. (2015). Adult attachment style is associated with cerebral μopioid receptor availability in humans. *Human Brain Mapping*, *36*(9), 3621–3628. https://doi.org/10.1002/hbm.22866
- Ompad, D. C., Ikeda, R. M., Shah, N., Fuller, C. M., Bailey, S., Morse, E., ... Vlahov, D. (2005). Childhood sexual abuse and age at initiation of injection drug use. *American Journal of Public Health*, 95(4), 703–709.
- R Core Team. (2017). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from https://www.Rproject.org/
- Reavis, J. A., Looman, J., Franco, K. A., & Rojas, B. (2013). Adverse Childhood
 Experiences and Adult Criminality: How Long Must We Live before We Possess
 Our Own Lives? *The Permanente Journal*, *17*(2), 44–48.
 https://doi.org/10.7812/TPP/12-072
- Renk, K., Boris, N. W., Kolomeyer, E., Lowell, A., Puff, J., Cunningham, A., ... McSwiggan, M. (2015). The state of evidence-based parenting interventions for parents who are substance-involved. *Pediatric Research*, 79(1–2), 177–183.

Rick, A. D., Vanheule, S., & Verhaeghe, P. (2009). Alcohol Addiction and the
Attachment System: An Empirical Study of Attachment Style, Alexithymia, and
Psychiatric Disorders in Alcoholic Inpatients. *Substance Use & Misuse*, 44(1),
99–114. https://doi.org/10.1080/10826080802525744

Rubin, D. B. (1976). Inference and missing data. *Biometrika*, 63(3), 581–592.

- Seth, P. (2018). Overdose Deaths Involving Opioids, Cocaine, and Psychostimulants United States, 2015–2016. MMWR. Morbidity and Mortality Weekly Report, 67. https://doi.org/10.15585/mmwr.mm6712a1
- Stan Development Team. (2018). Stan Modeling Language Users Guide and Reference Manual. Retrieved from http://mc-stan.org/users/documentation/
- Thorberg, F. A., & Lyvers, M. (2006). Attachment, fear of intimacy and differentiation of self among clients in substance disorder treatment facilities. *Addictive Behaviors*, 31(4), 732–737. https://doi.org/10.1016/j.addbeh.2005.05.050
- Tracy, K., & Wallace, S. P. (2016). Benefits of peer support groups in the treatment of addiction. Substance Abuse and Rehabilitation, 7, 143–154. https://doi.org/10.2147/SAR.S81535
- Ulmer, J. T., & Steffensmeier, D. (2014). The age and crime relationship: Social variation, social explanations. In *The nurture versus biosocial debate in criminology: On the origins of criminal behavior and criminality*. SAGE Publications Inc.
- van Buuren, S., & Groothuis-Oudshoorn, K. (2011). mice: Multivariate Imputation by Chained Equations in R. *Journal of Statistical Software*, *45*(3), 1–67.

Vehtari, A., Gelman, A., & Gabry, J. (2017). Practical Bayesian model evaluation using leave-one-out cross-validation and WAIC. *Statistics and Computing*, 27(5), 1413– 1432.

4.7 Exhibits

Demographic/Adversity	Prevalence	
Sample Size	352	
Female	31.0%	
Black	82.4%	
Recruited > 1988	73.3%	
Emotional Neglect	27.2%	
Physical Neglect	15.9%	
Lost Parent	37.7%	
Domestic Violence at Home	24.1%	
Household Member Drug Use	36.5%	
Household Member Mental Illness	26.3%	
Household Member Incarcerated	28.8%	
Peer Bullying	22.8%	
Social Isolation	29.8%	
Neighborhood Violence	52.3%	
Poverty	41.2%	
Emotional Abuse	20.2%	
Physical Abuse	20.8%	
Sexual Abuse	17.8%	

 Table 4.1. Adverse Childhood Experiences and Demographics of Baltimore City

 Adults who Have Injected Drugs

Note: Percents estimated from the average of 5 imputed datasets.

who have injected Drugs, by History of Adverse Childhood Experiences							
Outcome/Characteristic	All	0-1 Adversities 2	-4 Adversities	5+ Adversities			
Study Visits	8013	2770	2520	2723			
Heroin	39.9%	38.5%	38.0%	43.3%			
Cocaine	44.5%	43.3%	42.3%	47.7%			
Female	29.1%	30.5%	19.2%	36.7%			
Black	92.9%	92.4%	94.7%	91.9%			
cohort	48.5%	50.2%	51.1%	44.5%			
Visit 1980s	1.6%	1.9%	1.3%	1.7%			
Visit 1990s	21.1%	21.6%	20.4%	21.3%			
Visit 2000s	32.4%	32.6%	33.5%	31.2%			
Visit 2010s	44.9%	43.8%	44.8%	45.9%			

Table 4.2. Heroin and Cocaine Use and Characteristics of Baltimore City Adults who Have Injected Drugs, by History of Adverse Childhood Experiences

Note: Counts and percents estimated from the average of 5 imputed datasets.

Table 4.3. Estimated Mean Predicted Probability and Relative Odds of Heroin and Cocaine Use by Age and History of
Adverse Childhood Experiences

Age	0-1 Adversities		2-4 Adversities		3-5 Adversities	
	Probability	Odds Ratio v 0-1	Probability	Odds Ratio v 0-1	Probability	Odds Ratio v 0-1
Heroin						
35	87% (76.3% - 93.6%)	1 (1 - 1)	86.7% (75.4% - 93.4%)	0.97 (0.42 - 2.23)	72.4% (55.3% - 84.9%)	0.39 (0.17 - 0.88)
45	62.9% (47.7% - 77%)	1 (1 - 1)	62.4% (46.7% - 75.9%)	0.97 (0.44 - 2.11)	62% (45.4% - 76.3%)	0.95 (0.46 - 2.06)
55	22.3% (13.8% - 34.6%)	1 (1 - 1)	31.1% (19.7% - 45.3%)	1.56 (0.72 - 3.46)	48.1% (32.8% - 64.4%)	3.23 (1.51 - 7.08)
65	9.1% (4.2% - 18%)	1 (1 - 1)	7.9% (3.5% - 16.7%)	0.87 (0.3 - 2.59)	51.7% (30.4% - 72.5%)	10.71 (3.81 - 32.8)
Cocaine						
35	83.7% (70.9% - 91.9%)	1 (1 - 1)	82.2% (69.4% - 90.6%)	0.89 (0.4 - 2.03)	78% (63.4% - 88.5%)	0.69 (0.31 - 1.53)
45	65.3% (49.6% - 79%)	1 (1 - 1)	68.8% (54.5% - 80.7%)	1.16 (0.56 - 2.54)	60% (44.2% - 75.1%)	0.8 (0.37 - 1.72)
55	26.6% (16.3% - 40.5%)	1 (1 - 1)	33% (21.6% - 47.6%)	1.36 (0.64 - 2.97)	37.6% (24.4% - 54.3%)	1.68 (0.78 - 3.71)
65	4.6% (2.1% - 10%)	1 (1 - 1)	15.4% (7.3% - 29%)	3.73 (1.26 - 11.36)	43.1% (23.8% - 64.1%)	15.57 (5.15 - 45.92)

Note: Predictions for hypothetical male, Black participant, recruited in a post-1988 cohort, attending a study visit in the 2010s, with a random intercept of 0.

Note: Estimates based on average of 5 imputed datasets. Note: Results shown as – Bayesian Posterior Median (95% Bayesian Credible Interval)

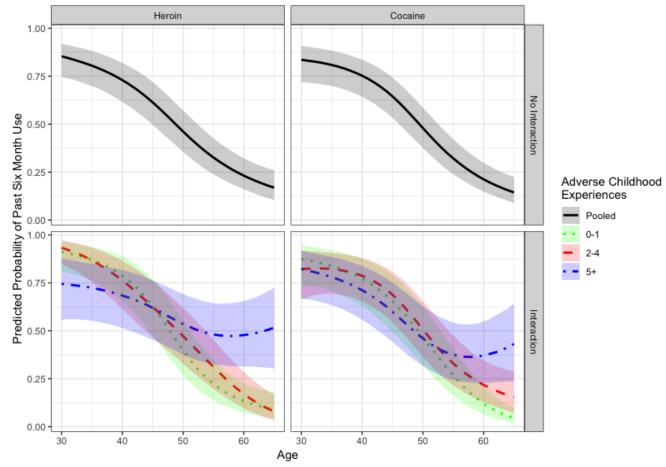


Figure 4.1 Estimated Predicted Probability of Heroin and Cocaine Use at Ages 30-65 by Exposure to Adverse Childhood Experiences in Baltimore Adults who Injected Drugs

Note: Predictions for hypothetical male, Black participant, recruited in a post-1988 cohort, attending a study visit in the 2010s, with a random intercept of 0. **Note:** Estimates based on average of 5 imputed datasets.

CHAPTER 5. VALIDATING BAYESIAN INTERRUPTED TIME-SERIES ANALYSIS TO STUDY FLORIDA'S OPIOID PRESCRIBING CRACKDOWN

5.0 Abstract

Background: In 2011, Florida established a Prescription Drug Monitoring Program and adopted new regulations for independent pain-management clinics. This chapter presents a method for examining the effects of those reforms on health outcomes in Florida, using the example of drug overdose deaths and other injury fatalities.

Methods: Florida's post-reform monthly mortality rates – for drug-involved deaths, motor vehicle crashes, and suicides by means other than poisoning – were compared to a counterfactual estimate of what those rates would have been absent reform. The counterfactual was estimated using a Bayesian structural time-series model based on mortality trends in similar states.

Results: By December 2013, drug overdose deaths were down -17% (95% CI, -21% to -12%), motor vehicle crash deaths were down -9% (-14%, to -4%), and suicide deaths were unchanged compared to what would be expected in the absence of reform.

Conclusion: Florida's opioid prescribing reform substantially reduced drug overdose deaths. Reforms may also have reduced motor vehicle crash deaths but had no effect on suicides; more research is needed to understand these patterns. Bayesian structural time-series modeling can be used for studying the effects of Florida's prescribing reforms on other outcomes, like child welfare involvement (Chapter 6).

5.1 Introduction

5.1.1 Florida Reforms Targeting Opioid Prescribing

Opioid overdose deaths in Florida consistently exceeded the national average from the 1990s into the late 2000s (National Institute on Drug Abuse, 2018). Identifying problematic opioid prescribing as a possible driver of these high overdose rates, in 2010-2011, Florida adopted a number of reforms to try to reduce prescription drug-related mortality.

First, Florida's legislature authorized the creation of a prescription drug monitoring program (PDMP). All prescribers of controlled substances were required to check the PDMP to review each patient's prescription history before prescribing a controlled substance, and log each prescription made in the PDMP. The law also allowed certain investigators from law enforcement and health agencies to access the PDMP (Gau et al., 2017).

Second, Florida's legislature officially defined "pain management clinics" to be programs that either advertised themselves as such or had a majority of their patients receiving pain medication. Florida required these programs to register with the state. Then, beginning July of 2011, Florida's adopted a "pill mill" law. This law required physician ownership of pain-management clinics, prohibited these clinics from operating onsite pharmacies, and permitted opioids to be prescribed only if the prescription was accompanied by a medical exam and follow-up care (Gau et al., 2017).

Following the adoption of these reforms, more than 500 of Florida's 900 independent pain management clinics closed (Gau et al., 2017). Opioid prescriptions fell as compared to other, similar states, with the largest reductions seen among doctors

making the highest volume of prescriptions and patients receiving the highest volume of prescriptions (Rutkow et al., 2015). Oxycodone overdose deaths fell sharply (Delcher, Wagenaar, Goldberger, Cook, & Maldonado-Molina, 2015), even as they continued to increase in nearby North Carolina (Kennedy-Hendricks et al., 2016).

Taken together, these studies suggest that Florida's policy changes were, at least initially, effective at achieving their primary objective – preventing unsafe opioid prescribing. There is also evidence that overdose deaths declined as a result of these measures.

5.1.2 Secondary Effects of Florida Policy on Other Injury Deaths

While overdose deaths have been the subject of past research, the effects of Florida's opioid prescribing reforms may not end at overdose deaths.

Opioid use can induce drowsiness and impair cognitive function (Altilio et al., 2007). This could increase risk for car crashes. In fact, opioid use is associated with unsafe driving behavior among people involved in motor vehicle crashes (Dubois, Bédard, & Weaver, 2010). Further, among people drug-tested following motor vehicle crashes, the proportion identified as having used opioids has increased over the last decade (Governors Highway Safety Assocation, 2018). However, at least one literature review found no evidence that opioid use was associated with motor vehicle crashes. (Fishbain, Cutler, Rosomoff, & Rosomoff, 2002).

Further, some critics of restrictions on opioid prescribing argue that crackdowns on opioid prescribing may lead to poor management of chronic pain and, in some cases, increased risk for suicide (Levine, 2018). Chronic pain is associated increased risk for suicide attempt and completion (Racine, 2018), and very high rates of suicidal ideation

and attempt have been found among veterans whose physicians terminated their prescription opioid use (Demidenko et al., 2017).

In summary, in addition to drug overdose deaths, it is plausible that Florida's opioid crackdown might have affected rates of death from motor vehicle crash and suicide. To date, no studies have examined the effect of Florida's opioid prescribing reforms – or any other legal intervention targeting opioid prescribing – on these other possible sources of injury mortality.

5.1.3 Motivation and Hypotheses

This study examines the effect of Florida's PDMP and pill mill laws on mortality in Florida. Past research on mortality trends following Florida's prescribing reforms has focused only on mortality from drug overdoses. Those analyses have also been limited by the absence of a strong control group – studies relied either on a single comparison state (Kennedy-Hendricks et al., 2016) or included no comparison state at all (Delcher et al., 2015). Here, we first seek to replicate the finding that drug overdose deaths declined dramatically following Florida's prescribing reform using Bayesian structural time series models (BSTS), a relatively new approach to interrupted time series that allows for the inclusion of multiple states and allows for adjustment for local or seasonal trends observed in the pre-intervention period. Next, we extend those results to two other possible causes of mortality that could be affected by prescribing reforms – motor vehicle crashes and suicide deaths not caused by poisoning. As a control, we also examine the effect of Florida's reform on two causes of mortality – major cardiovascular diseases and malignant neoplasms – that should not be affected.

We hypothesize that, in the two-and-a-half years following Florida's prescribing reforms, drug overdose and motor vehicle crash deaths all declined, but suicide deaths increased, relative to what would have occurred had Florida not instituted any reforms. We hypothesize no change the control outcomes, heart disease or cancer.

In the context of this dissertation, a secondary goal of this study is to demonstrate the utility of a new approach to analyzing interrupted time series data – Bayesian structural time series. By replicating the previously demonstrated reduction in opioid mortality following Florida's prescribing reforms, we establish the utility of this method for seeing if Florida's prescribing reform had the unintended benefit of reducing substantiated child maltreatment (Chapter 6).

5.2 Methods

5.2.1 Data

Monthly mortality counts were extracted for Florida and all states using data from publicly available counts published through the CDC's online WONDER database. (Centers for Disease Control and Prevention, National Center for Health Statistics., 2017). The WONDER database can be found at https://wonder.cdc.gov/. Drug overdose deaths include all deaths where the underlying cause of death was determined to be drug-related. Note that this could include accidental overdoses, suicides, or homicides. Suicide deaths include all injury deaths where the injury intent was determined to be suicide, excluding deaths where the mechanism of injury was poisoning. Poisoning deaths were excluded to distinguish this outcome from the drug overdose deaths outcome and isolate suicide deaths that were not caused by drug overdose (but see 2.3.7 "Sensitivity Analysis"). Motor vehicle crash, as well as the two control outcomes major

cardiovascular disease and *malignant neoplasm* deaths, each included all deaths in the corresponding "113 Causes of Death" type. To compute monthly mortality rates, these counts were divided by annual average population totals taken from U.S. Census intercensal estimates of the population of each state. These estimates can be found on the Census bureau's FTP site (<u>https://www2.census.gov/programs-surveys/popest/</u>).

5.2.2 Study Sample

The time period for this study is January, 2005 through December, 2013. Twentythree states were selected as possible states because they already had some type of PDMP law in place as early as 2005. These states were identified using the Law Atlas project from the Policy Surveillance Program at Temple University School of Law (NPO Staff, 2018). Restricting states to states with a PDMP in 2005 was necessary because, in order to serve as comparisons, states could not have made a similar policy change to Florida (see the "Assumptions" section). (We considered using states that *did not* have a PDMP for the entire observation period as comparison states; it turned out that there were no states that met this criterion.).

The CDC suppresses the monthly mortality count for each state reporting fewer than 10 deaths in that month. For this reason, in the analysis of each cause of death, some of the 23 eligible comparison states were not actually included as comparisons because at least one of their mortality totals was suppressed. The exact comparison states included in each analysis are shown in Table 1. Every analysis had at least 17 comparison states.

5.2.3 Analytic Approach

The goal of the analysis is to determine how different Florida's mortality rate for each cause of injury mortality would have been had it not adopted the opioid prescribing reforms described above (hereafter the "intervention"). The analytic approach is the same for all mortality measures, so from here we refer generally to the "mortality rate." We can only observe Florida's behavior in the presence of the intervention, so the goal is to estimate Florida's behavior in the absence of intervention. There are three natural approaches to estimating how Florida would have behaved in the post-intervention period: 1) we could extrapolate from Florida's behavior in the pre-intervention period; 2) we could infer Florida's behavior in the post-intervention period; 3) we could use our prior assumptions about how Florida should have behaved in the post-intervention period (Brodersen, Gallusser, Koehler, Remy, & Scott, 2015). We adopt the approach described by Brodersen and colleagues (Brodersen et al., 2015), and combine all three sources of information using a method known as Bayesian Structural Time Series (BSTS) models to forecast Florida's behavior in the absence of the intervention. By taking the difference between our forecast and the observed value, we estimate the effect of the intervention.

Below, we briefly describe BSTS models and describe their application to the problem at hand. BSTS models are described elsewhere in detail (Brodersen et al., 2015; Scott, 2017; Scott & Varian, 2014)

5.2.3.1 Brief Background on Bayesian Modeling. All Bayesian models have three components: 1) a "prior" probability distribution that quantifies existing beliefs about each parameter of interest before data are collected; 2) a "likelihood" that quantifies the probability of the observed data given the parameters of interest; and 3) a "posterior" distribution that combines the prior and the likelihood using Bayes' theorem to combine information (from the prior and the data) about each parameter of interest.

Inference is made by summarizing the posterior distribution – for example, instead of a traditional frequentist "point estimate" of a parameter, a Bayesian estimate might be the mean (or median) of the posterior distribution for that parameter. Bayesian methods allow for extremely flexible interpretation of model parameters because, so long as we can sample from the posterior distribution of model parameters, we can also estimate the posterior for any arbitrary combination of those parameters through Monte Carlo simulation. In practice, it is often impossible to sample directly from the posterior distribution, in which case Markov Chain Monte Carlo (MCMC) methods are used to sample indirectly. In this analysis, each time we fit a model, we went through 10,000 MCMC iterations to estimate the posterior. For an introduction to Bayesian methods, see van de Schoot and colleagues (van de Schoot et al., 2014).

5.2.3.2 Bayesian Structural Time Series Models (BSTS). BSTS use the flexibility of Bayesian model averaging to combine a number of different time series models into a single forecast. In this analysis, we average two simple models for Florida's behavior in the post-intervention period:

- 1. The first is a seasonal model, where Florida's mortality rate is modeled using a dummy variable for three-month periods (e.g., Jan-Mar, Apr-Jun, etc).
- 2. The second is a "spike-and-slab" linear regression model (Ishwaran & Rao, 2005), where Florida's mortality rate in each month of the pre-intervention period is regressed on the mortality rate in the comparison states. Spike-and-slab regression is a machine-learning approach similar to lasso or ridge regression that uses "shrinkage" to down-weight covariates that do less to improve predictive

accuracy, reducing model variance and improving out-of-sample predictions as compared a simple linear regression (Ishwaran & Rao, 2005).

The averaged model is then used to generate regression predictions of Florida's mortality rates in the post-intervention period based on seasonal trends and the behavior of the comparison states in the post-intervention period.

5.2.3.3 Model Fitting. Bayesian models require specification of a prior for all parameters. To all regression coefficients, seasonal dummy variables, and residual variances, we assign so-called "non-informative" prior distributions, a common default choice in Bayesian analysis, and the default in the modeling package used (see "Software"). These are consistent with the fact that we have essentially no *a priori* knowledge as to what these parameters should be. The spike and slab model also requires a meta-parameter – the "expected model size" – to be chosen. We chose an expected model size of 1. This technically corresponds to a prior belief that there is a 1/n probability that each regressor is predictive of the mortality rate in Florida; more practically, the prior functions as a form of "shrinkage" to reduce model variance and improve accuracy similar to a "lasso" or "ridge regression." This is a conservative prior choice, because it does presume any state is more or less predictive, and is the default for the modeling package used (see "Software").

5.2.3.4 Effect Estimation. We fit a BSTS to forecast Florida's mortality rate in the post-intervention period. For each MCMC iteration, for all months in the post-intervention period, we convert predicted rates into counts and take the difference between the observed death count and the model-estimated death count – this is an estimate of the effect of the intervention in that month. In addition to these monthly

estimates, we add the model-estimated monthly count to the model-estimated count in all prior months, and take the difference between this model-estimated value and observed value – this is an estimate of the cumulative effect of the intervention up to that month. Taking the mean and 0.025 and 0.975 quantiles of these posteriors give point estimates and 95% Bayesian credible intervals for the effect of the intervention up through each post-intervention point.

5.2.3.5 Model Checking and Inference. The analysis relies heavily on the assumption that any deviation between our forecast of Florida's post-intervention mortality rate and its true post-intervention rate is attributable to the effect of the intervention, and not model mis-specification. We test the plausibility of this assumption two ways:

First, we use a simplified version of the test proposed by Abadie and colleagues (Abadie et al., 2010). Specifically, we repeat the same analysis on each of the comparison states, and rank the estimated relative change in number of incidents in each state from the largest to the smallest magnitude. Since comparison states did not adopt any intervention during the observation period, estimated "intervention effects" should be zero in expectation, and much smaller than those observed in Florida. If intervention effects estimated in Florida are comparable in magnitude to those observed in the comparison states, then we would be concerned these effects are merely the result of random error or model misspecification.

Second, we repeat the entire analysis for two causes of mortality that should not have been affected by Florida's prescribing reform – major cardiovascular diseases, and malignant neoplasms. If the modeling approach cannot accurately predict post-

intervention trends in these unaffected causes of death, then we would be concerned than any effects observed on the outcomes of interest were merely the result of the poor predictive accuracy of the model.

5.2.3.6 Assumptions. The first important assumption underlying this analysis is that Florida's PDMP and pill mill laws had no effect on the outcome in any comparison state (i.e., the Stable Unit Treatment Value Assumption, or SUTVA). This assumption could be violated if, for example, these laws reduced illegal trafficking of opioids from Florida to other states used as comparisons. The second assumption is that, had Florida not adopted its PDMP and pill mill laws, the association between mortality in comparison states and Florida before July 2011 would have remained the same after July 2011. This assumption would be violated if, for example, a comparison state adopted some other reform that caused its mortality rate to diverge from Florida's.

5.2.3.7 Sensitivity Analysis – Poisoning Suicide. As noted, the estimated suicide death rate excluded deaths caused by poisoning, which might be affected differently than other methods of suicide. As a sensitivity analysis, we repeated our analysis of suicides including all suicides, including poisoning.

5.2.3.8 Software. All models were estimating using the "bsts" package in R (R Core Team, 2017; Scott, 2017).

5.3 Results

5.3.1 Drug Overdose

Drug overdose deaths in Florida increased from 2005 into 2011, before declining by the end of 2013 (Table 2, Figure 1). As compared to the BSTS-estimated counterfactual estimates, by December of 2013, cumulative drug overdose deaths over

the full observation period were down by about a sixth (-16.8%, 95% Credible Interval - 21.3% to -11.7%) (Table 3, Figure 2). This corresponds to a reduction of 1,377 deaths, or an average of 86 deaths averted per month.

5.3.2 Motor Vehicle Crash

Motor vehicle crash deaths declined from 2005 into 2011, before increasing slightly by the end of 2013 (Table 2, Figure 1). As compared to the BSTS-estimated counterfactual estimates, cumulative motor vehicle crash deaths over the full observation period were down by about a tenth (-9.1%, 95% CI -14.4% to -3.5%) (Table 3, Figure 2). This corresponds to a reduction of 615 deaths, or an average of 38 deaths averted per month.

5.3.3 Suicide

Non-poisoning suicide deaths fluctuated over the study period (Table 2, Figure 1). As compared to the BSTS counterfactual estimates, suicides were essentially unchanged (0.4%, 95% CI -7.0% to 8.3%) (Table 3, Figure 2). Results of sensitivity analysis where poisoning suicides were included were the same (not shown).

5.3.4 Model Checking

After repeating the analysis in all comparison states, the magnitude of the percent change in cause-specific mortality at 30 months in Florida was the third (out of 18) largest for drug overdose, third (out of 18) for motor vehicle crash, and 17th (out of 18) for suicide (Appendix Exhibits, Figures 1-4). In other words, the intervention effect in Florida on both drug overdose and motor vehicle crash death, but not suicide, was more extreme than "effects" observed by chance in most other states that did not actually implement any intervention (Table 3).

Repeating the analysis for major cardiovascular disease and malignant neoplasm mortality showed no effect of prescribing reforms on these control outcomes (Appendix Exhibits, Figures 5 and 6).

5.4. Discussion

5.4.1 Drug Overdose Deaths

Our analysis provides strong evidence that policies that reduce high-volume or insufficiently supervised opioid prescribing prevent drug overdose deaths. We find that drug overdose mortality declined sharply following the introduction for Florida's opioid prescribing reforms, preventing 1,377 drug overdose deaths during the 30 months following of the introduction of the pill mill law. This is similar to the conclusions of Kennedy-Hendricks and colleagues (Kennedy-Hendricks et al., 2016), who analyzed a slightly different 34 month period and found reforms prevented 1,029 prescription opioid overdose deaths. Our analysis has a number of unique strengths: Our analytic approach combines information from 17 comparison states (instead of only one) and from seasonal patterns in the pre-intervention period to produce precise estimates. We also verify the predictive accuracy of our modeling approach in states that did not implement any intervention, and with other sources of mortality in Florida that should be unaffected by prescribing reforms. Finally, we include all drug overdose mortality, rather than trying to distinguish between sources of mortality, because there is evidence that incomplete cause-of-death reporting leads to undercounts of opioid-specific mortality (Buchanich, Balmert, Williams, & Burke, 2018). We find it encouraging that these two studies – which used different data sources and different analytic approaches - reached very similar conclusions.

It is important to note that we (and Kennedy-Hendricks et al.) ended our observation period at the end of 2013. Beginning in 2014, deaths from synthetic opioids such as fentanyl increased dramatically. Synthetics quickly became the leading cause of opioid overdose death, both in Florida and nationally, and annual drug overdose deaths more than doubled (National Institute on Drug Abuse, 2017). We cannot be sure that the benefits of Florida's prescribing reforms were sustained in this new era of synthetic opioids. However, we find it encouraging that our monthly estimates (Figure 2) suggest that all drug overdose deaths were consistently down over our entire two-and-a-half-year study period – this suggests that prescribing reforms did not lead opioid users to immediately substitute other, illegal drugs.

We should also note that our ecological approach does not provide any information about why Florida's reforms were effective. Prescribing reforms could prevent mortality in a number of ways: by preventing accidental overdoses of people receiving an opioid prescription who have no addiction; by preventing accidental overdoses of people receiving an opioid prescription who misuse their drugs or have an addiction; by preventing the formation of new opioid addictions; by preventing druginduced suicide deaths; or by preventing diversion of drugs onto the black market. We also cannot determine who was affected by the reform – older or younger opioid users, men or women, or people living in urban or rural areas. Understanding who is affected and mechanism of action is essential to developing and targeting new policies that meet the needs of people who may not be benefitting from prescribing reforms; this is an important topic for future research.

5.4.2 Other Sources of Mortality

In addition to drug overdose death, we were interested in how Florida's prescribing reforms might have affected other causes of death that may be linked to opioid use. Our findings were mixed:

Our model estimates an approximately 9 percent reduction in motor vehicle crash fatalities attributable to Florida's prescribing reforms. This is consistent with our hypothesis that fewer opioid prescriptions would lead to less opioid-impaired driving. However, unlike drug overdose deaths – which fell almost immediately in the second half of 2011 – most of this reduction comes from lower than expected rates of motor vehicle crash death in 2013. We did not anticipate this delayed effect *a priori*. Further, we did not directly examine drug-impaired driving. Therefore, we would consider these findings preliminary, and believe they should motivate future research on opioids and driving.

By contrast, we find no evidence that suicide mortality changed following Florida's opioid prescribing reforms. This was true both of all suicides, and of all suicides other than poisonings. This is encouraging, because both medical organizations and the popular press have raised concerns that prescribing reforms may lead to increased suicide deaths among people whose pain was previously treated by opioids (Kertesz, Manhapra, Olivia, & Sandbrink, 2018; Levine, 2018). Opioid prescribing has declined across the country since 2011 (IQVIA, 2018), a process that has likely accelerated due to new CDC guidelines on opioid prescribing (Dowell, Haegerich, & Chou, 2016). While careful monitoring of these broader declines and of the appropriateness of CDC guidelines is needed, it is encouraging that, even after Florida's dramatic reforms to opioid prescribing, suicide rates did not budge relative to other, similar states.

5.4.3 New Methods for Interrupted Time Series

In addition to substantive findings, this study presents an application of a relatively new analytic approach – Bayesian structural time series (BSTS) models for causal impact evaluation. Although BSTS models have been used in some public health settings (Bruhn et al., 2017), we believe these models are likely unfamiliar to many epidemiologists and wish to highlight some of their benefits and compare them to other approaches commonly used in epidemiology for causal impact evaluation:

- BSTS models improve predictive accuracy by combining information from trends in the target unit seen in the preintervention period with the observed behavior of other similar comparison units that did not receive the intervention in the postintervention period. This combines the strengths of two other common approaches to these problems – time series models like ARIMA, and difference-in-difference approaches like panel regression (Bernal, Cummins, & Gasparrini, 2017; Card & Krueger, 1994).
- 2. BSTS models also improve predictive accuracy by not treating all comparison units as equally useful. Instead, BSTS uses "machine learning" (spike-and-slab regression) to place more weight on comparison units that best predict the behavior of the intervention unit in the pre-intervention period.
- 3. By predicting post-intervention trends from the observed behavior of comparison units, BSTS models do not require any parametric assumptions about postintervention trends (e.g., that they will be linear or quadratic).
- 4. Because BSTS models make predictions at every timepoint in the postintervention period, it is possible to accurately estimate a wide variety of effects that may be scientifically interesting. For example, we can estimate the effect of

the intervention in any particular month (e.g., Figure 2, left side) or the cumulative effect of the intervention up to any particular month (e.g., Figure 2, right side).

- 5. BSTS models are Bayesian, which means that they produce a full posterior distribution for every estimated quantity. This also means that, for any effect we estimate, we can also construct a 95% interval of uncertainty. This is not true of some other more flexible interrupted time series designs like synthetic control methods (Abadie et al., 2010).
- 6. Estimating the treatment effect in one unit based on other comparison units lends itself to a natural and transparent model-checking approach. Since comparison units implement no intervention, it should be possible to predict their behavior in the post-intervention period accurately. If predictions in comparison states are poor, then it is likely that estimated intervention effects are wrong.
- 7. BSTS models are automated in a user-friendly R package (Scott, 2017). Further, although not used in this paper, interrupted time series analysis with BSTS is also automated in a user-friendly package (Brodersen et al., 2015). Both of these packages provide automated tools for visualizing models, which can help users make thoughtful modeling decisions, check that predictions are consistent with data, and present results in an intuitive format.

The analysis above illustrates all of these properties and can serve as a model for a diverse array of epidemiologic investigations.

5.4.4 Limitations

This analysis has a number of limitations. First, the main assumption of our analysis is that Florida's PDMP and pill mill laws were the only state interventions that might have impacted the mortality rates analyzed here. We cannot know if some other policy change made in Florida or in one of the comparison states highly predictive of Florida's pre-intervention trends is responsible for the effects described here. Second, mortality rates are estimated by dividing CDC reported monthly counts by census mean annual population estimates. Since the population changes over the course of the year, there is some error in these estimated rates, although likely very small. Third, this is an ecological study, and the outcome analyzed is a rate calculated at the state level – research on individuals is needed to determine the effects of reducing or eliminating opioid use on individual risk for the types of mortality examined here.

5.5 Conclusion

The analysis presented here offers strong evidence that Florida's opioid prescribing reforms sharply reduced drug overdose deaths over the thirty-month period following their introduction. It also offers comforting evidence that Florida's suicide mortality rate did not change following these reforms. Finally, the analysis offers preliminary evidence that prescribing reforms may have reduced motor vehicle crash fatality – possibly because of reductions in opioid-impaired driving. These final two results merit further investigation with data collected from individuals who currently use or formerly used opioids.

For policy-makers, we think there are two clear implications. First, reforms that reduce irresponsible or unnecessary opioid prescribing prevent drug overdose deaths. States and the federal government should continue to promulgate regulations that reduce

prescribing of opioids and promote alternative treatment of chronic pain. Second, these reforms may have unanticipated consequences. In this study, we identified a possible positive unintended consequence – a reduction in motor vehicle crash deaths – without any negative unintended consequences – a change in suicide deaths. However, other reforms structured differently might have different effects on different outcomes. It will be important carefully monitor pain patients in locations instituting opioid prescribing reforms on multiple outcomes, to ensure that any reduced risk of overdose death is accompanied by overall reductions in morbidity and mortality risk.

For researchers, it will be important to understand who has been affected by Florida's opioid prescribing reforms and why the law has been effective. The findings presented here also should remind researchers that it is important to examine not only the targeted outcome of drug control policies, but also secondary and possibly negative outcomes, to ensure the benefits of policy change outweigh the harms.

Finally, the method we present here – BSTS for causal impact analysis – is an excellent tool for studying both the intended and collateral impacts of state-level drug policies. Interrupted time series analyses are plagued by contradictory or implausible findings. For example, two recent studies published within months of each other found large but opposite effects of laws permitting bystanders to carry naloxone on opioid misuse (Doleac & Mukherjee, 2018; Rees, Sabia, Argys, Latshaw, & Dave, 2017). Subsequent research suggests that naloxone use did not increase in these states following the introduction of these laws, making both findings implausible (Frank, Humphreys, & Pollack, 2018). We believe BSTS can help reduce these kinds of contradictory findings by forcing researchers to clearly display the results of their modeling in a way that is

easily understandable to a general scientific audience – because it focuses on isolating the effect of a single intervention in a single state, because its results are easily visualized, and because it facilitates intuitive model-checking through repeated analysis of comparison states.

5.6 References

- Abadie, A., Diamond, A., & Hainmueller, J. (2010). Synthetic control methods for comparative case studies: Estimating the effect of California's tobacco control program. *Journal of the American Statistical Association*, 105(490), 493–505.
- Altilio, T., Brennan, M., Dahl, J., Edwards, A., Fouladbakhsh, J., & Keefe, F. (2007).
 Treatment Options: A Guide for People Living with Pain. *Baltimore, MD: American Pain Foundation*.
- Bernal, J. L., Cummins, S., & Gasparrini, A. (2017). Interrupted time series regression for the evaluation of public health interventions: a tutorial. *International Journal* of Epidemiology, 46(1), 348–355. https://doi.org/10.1093/ije/dyw098
- Brodersen, K. H., Gallusser, F., Koehler, J., Remy, N., & Scott, S. L. (2015). Inferring causal impact using Bayesian structural time-series models. Retrieved from https://research.google.com/pubs/pub41854.html
- Bruhn, C. A. W., Hetterich, S., Schuck-Paim, C., Kürüm, E., Taylor, R. J., Lustig, R., ... Weinberger, D. M. (2017). Estimating the population-level impact of vaccines using synthetic controls. *Proceedings of the National Academy of Sciences*, *114*(7), 1524–1529. https://doi.org/10.1073/pnas.1612833114
- Buchanich, J. M., Balmert, L. C., Williams, K. E., & Burke, D. S. (2018). The Effect of Incomplete Death Certificates on Estimates of Unintentional Opioid-Related Overdose Deaths in the United States, 1999-2015. *Public Health Reports (Washington, D.C.: 1974)*, *133*(4), 423–431. https://doi.org/10.1177/0033354918774330

- Card, D., & Krueger, A. B. (1994). Minimum Wages and Employment: A Case Study of the Fast-Food Industry in New Jersey and Pennsylvania. *The American Economic Review*, 84(4), 772–793.
- Centers for Disease Control and Prevention, National Center for Health Statistics. (2017). *Underlying Cause of Death 1999-2016 on CDC WONDER Online Database, released December, 2017. Data are from the Multiple Cause of Death Files, 1999-2016, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program.* Retrieved from http://wonder.cdc.gov/ucd-icd10.html
- Delcher, C., Wagenaar, A. C., Goldberger, B. A., Cook, R. L., & Maldonado-Molina, M. M. (2015). Abrupt decline in oxycodone-caused mortality after implementation of Florida's Prescription Drug Monitoring Program. *Drug and Alcohol Dependence*, *150*, 63–68. https://doi.org/10.1016/j.drugalcdep.2015.02.010
- Demidenko, M. I., Dobscha, S. K., Morasco, B. J., Meath, T. H. A., Ilgen, M. A., & Lovejoy, T. I. (2017). Suicidal ideation and suicidal self-directed violence following clinician-initiated prescription opioid discontinuation among long-term opioid users. *General Hospital Psychiatry*, 47, 29–35. https://doi.org/10.1016/j.genhosppsych.2017.04.011

 Doleac, J. L., & Mukherjee, A. (2018). *The Moral Hazard of Lifesaving Innovations: Naloxone Access, Opioid Abuse, and Crime* (SSRN Scholarly Paper No. ID 3135264). Rochester, NY: Social Science Research Network. Retrieved from https://papers.ssrn.com/abstract=3135264

- Dowell, D., Haegerich, T. M., & Chou, R. (2016). CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR. Recommendations and Reports, 65. https://doi.org/10.15585/mmwr.rr6501e1er
- Dubois, S., Bédard, M., & Weaver, B. (2010). The association between opioid analgesics and unsafe driving actions preceding fatal crashes. *Accident Analysis & Prevention*, 42(1), 30–37. https://doi.org/10.1016/j.aap.2009.06.030
- Fishbain, D. A., Cutler, R. B., Rosomoff, H. L., & Rosomoff, R. S. (2002). Can Patients Taking Opioids Drive Safely?? *Journal of Pain & Palliative Care Pharmacotherapy*, 16(1), 9–28. https://doi.org/10.1080/J354v16n01_03
- Frank, R. G., Humphreys, K., & Pollack, H. A. (2018, March 19). Does NaloxoneAvailability Increase Opioid Abuse? The Case for Skepticism. Retrieved April 23, 2018, from

https://www.healthaffairs.org/do/10.1377/hblog20180316.599095/full/#.Wq_oPlJ aD2c.twitter

Gau, J. M., Moreto, W. D., Potter, R. H., Brooke, E. J., Florida, U. of C., & America, U.
S. of. (2017). Non-medical Use of Prescription Drugs: Policy Change, Law
Enforcement Activity, and Diversion Tactics. Department of Criminal Justice,
University of Central Florida.

Governors Highway Safety Assocation. (2018). Drug Impaired Driving: Marijuana and Opioids Raise Critical Issues for States. Retrieved from https://www.insurancejournal.com/app/uploads/2018/05/GHSA_DrugImpairedDri ving_FINAL-1.pdf

- IQVIA. (2018). Medicine Use and Spending in the U.S.: A Review of 2017 and Outlook to 2022. Retrieved from https://www.iqvia.com/institute/reports/medicine-useand-spending-in-the-us-review-of-2017-outlook-to-2022
- Ishwaran, H., & Rao, J. S. (2005). Spike and slab variable selection: frequentist and Bayesian strategies. *The Annals of Statistics*, *33*(2), 730–773.

Kennedy-Hendricks, A., Richey, M., McGinty, E. E., Stuart, E. A., Barry, C. L., & Webster, D. W. (2016). Opioid Overdose Deaths and Florida's Crackdown on Pill Mills. *American Journal of Public Health*, *106*(2), 291–297. https://doi.org/10.2105/AJPH.2015.302953

- Kertesz, S., Manhapra, A., Olivia, E., & Sandbrink, F. (2018, April). VA Data about Prescription Opioids and Overdose and Suicide: Clinical Implications. Presented at the National Prescription Drug Abuse and Heroin Summit. Retrieved from https://www.scribd.com/document/375496421/VA-April-4th-Data-Opioids-Suicides
- Kolodny, A., Courtwright, D. T., Hwang, C. S., Kreiner, P., Eadie, J. L., Clark, T. W., & Alexander, G. C. (2015). The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. *Annual Review of Public Health*, *36*, 559–574.

Levine, A. (2018, July 31). The Government's Solution To The Opioid Crisis Feels Like A War To Pain Patients. Retrieved from https://www.huffingtonpost.com/entry/government-crackdown-opioidprescriptions-pain-patients_us_5b51ec57e4b0fd5c73c4a42e

- National Institute on Drug Abuse. (2017, September 15). Overdose Death Rates. Retrieved February 19, 2018, from https://www.drugabuse.gov/relatedtopics/trends-statistics/overdose-death-rates
- National Institute on Drug Abuse. (2018, February 28). Florida Opioid Summary. Retrieved June 29, 2018, from https://www.drugabuse.gov/drugsabuse/opioids/opioid-summaries-by-state/florida-opioid-summary
- NPO Staff. (2018, July). LawAtlas Policy Surveillance Report, Query Report on Dataset: Query where At least one of these selections apply - Does this state have legislation authorizing access by professionals to a PDMP system? Retrieved from lawaltas.org/preview?dataset=prescription-monitoring-program-laws-1408223332
- R Core Team. (2017). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from https://www.Rproject.org/
- Racine, M. (2018). Chronic pain and suicide risk: A comprehensive review. Progress in Neuro-Psychopharmacology & Biological Psychiatry, 87(Pt B), 269–280. https://doi.org/10.1016/j.pnpbp.2017.08.020
- Rees, D. I., Sabia, J. J., Argys, L. M., Latshaw, J., & Dave, D. (2017). With a Little Help from My Friends: The Effects of Naloxone Access and Good Samaritan Laws on Opioid-Related Deaths (Working Paper No. 23171). National Bureau of Economic Research. https://doi.org/10.3386/w23171
- Rutkow, L., Chang, H.-Y., Daubresse, M., Webster, D. W., Stuart, E. A., & Alexander,G. C. (2015). Effect of Florida's Prescription Drug Monitoring Program and Pill

Mill Laws on Opioid Prescribing and Use. *JAMA Internal Medicine*, *175*(10), 1642. https://doi.org/10.1001/jamainternmed.2015.3931

- Scott, S. L. (2017, July 11). Fitting Bayesian structural time series with the bsts R package. Retrieved from http://www.unofficialgoogledatascience.com/2017/07/fitting-bayesian-structuraltime-series.html
- Scott, S. L., & Varian, H. R. (2014). Predicting the present with bayesian structural time series. *International Journal of Mathematical Modelling and Numerical Optimisation*, 5(1–2), 4–23.
- van de Schoot, R., Kaplan, D., Denissen, J., Asendorpf, J. B., Neyer, F. J., & van Aken, M. A. G. (2014). A gentle introduction to bayesian analysis: applications to developmental research. *Child Development*, 85(3), 842–860. https://doi.org/10.1111/cdev.12169

	Comparison States Incl	uucu in Each Analysis		Major	
		Motor Vehicle		Cardiovascular	Malignant
	Drug Overdose	Crash	Suicide	Disease	Neoplasm
AL	X	Х	Х	Х	X
CA	Х	Х	Х	Х	Х
CO	Х	Х	Х	Х	Х
FL	Х	Х	Х	Х	Х
HI				Х	Х
ID				Х	Х
IL	Х	Х	Х	Х	Х
IN	Х	Х	Х	Х	Х
KY	Х	Х	Х	Х	Х
ME				Х	Х
MA	Х	Х	Х	Х	Х
MI	Х	Х	Х	Х	Х
NV	Х	Х	Х	Х	Х
NM	Х	Х		Х	Х
NY	Х	Х	Х	Х	Х
OH	Х	Х	Х	Х	Х
OK	Х	Х	Х	Х	Х
PA	Х	Х	Х	Х	Х
RI				Х	Х
TX	Х	Х	Х	Х	Х
UT	Х		Х	Х	Х
VA	Х	Х	Х	Х	Х
WV		Х	Х	Х	Х
WY				Х	Х

5.7 Exhibits

Table 5.1 /	Comparison	States	Included	in Fach	Analysis
1 apre 3.1. v	Comparison	States	Included	п сасп	Allalysis

Note: "X" indicates the state was included.

Clackdown Deginn	ing July 2011				
	Drug	Motor Vehicle		Major Cardiovascular	Malignant
Month	Overdose	Crash	Suicide	Disease	Neoplasm
January, 2005	1.1 (197)	1.7 (310)	0.9 (156)	30.9 (5522)	19.2 (3417)
July, 2011	1.4 (274)	1.1 (202)	1.1 (204)	22.3 (4254)	18.5 (3520)
December, 2013	1.2 (233)	1.2 (232)	0.9 (182)	25.1 (4898)	18.5 (3618)

 Table 5.2. Monthly Drug and Other Cause Mortality Rates and Counts Before and After Florida's Opioid Prescribing

 Crackdown Beginning July 2011

Note: Rate is deaths per 100,000 residents per month.

2011-0uly 2014			
	July, 2011 through December, 2011	July, 2011 through December, 2012	July, 2011 through December, 2013
	Determoer, 2011	Determoer, 2012	December, 2015
Drug Overdose	-5.9% (-12.9% to 2.3%)	-13.6% (-18.6% to -7.8%)	-16.8% (-21.2% to -11.8%)
Motor Vehicle Crash	-5.6% (-15.5% to 5.7%)	-6.2% (-12.5% to 0.6%)	-9.1% (-14.5% to -3.6%)
Suicide (non-poisoning)	-0.3% (-9.8% to 10.7%)	0.2% (-8.5% to 9.4%)	0.4% (-7% to 8.3%)
Major Cardiovascular Disease	-1.2% (-4.7% to 2.6%)	-0.4% (-2.7% to 2.2%)	-0.7% (-2.7% to 1.7%)
Malignant Neoplasm	0.3% (-1.8% to 2.4%)	-0.2% (-1.5% to 1.1%)	0.1% (-1.1% to 1.3%)

Table 5.3. Estimated Cumulative Percent Change in Mortality following Florida's Opioid Prescribing Crackdown, July2011-July 2014

Effects presented as: Estimate (95% Credible Interval)

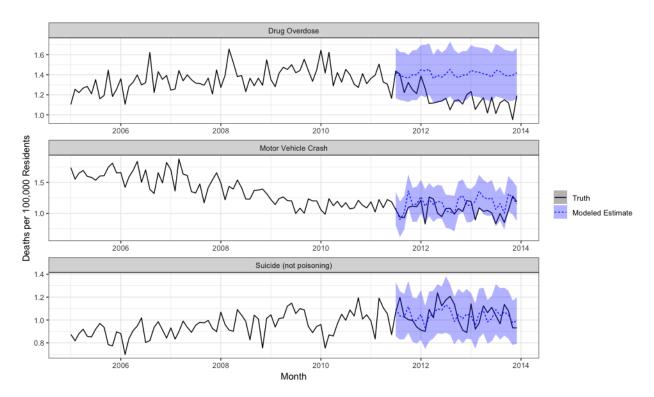


Figure 5.1. Rates of Observed and Model-Estimated Mortality in Florida, 2005-2014.

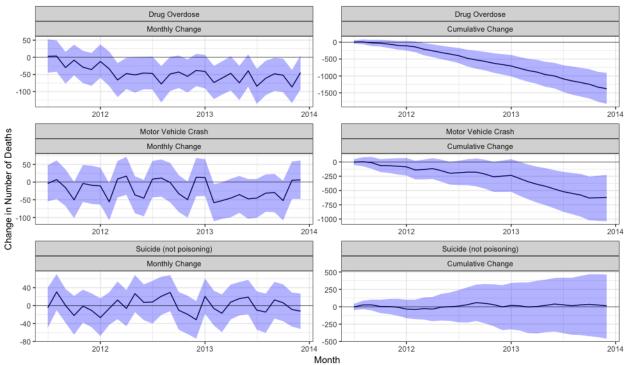


Figure 5.2. Estimated Change in Mortality following Florida Opioid Prescribing Reform

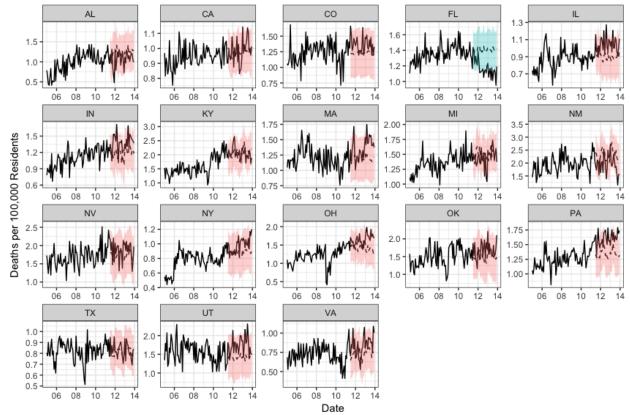


Figure 5.1a. Estimated Effect of Florida Opioid Prescribing Crackdown on Drug Overdose Deaths: Florida vs Comparison States

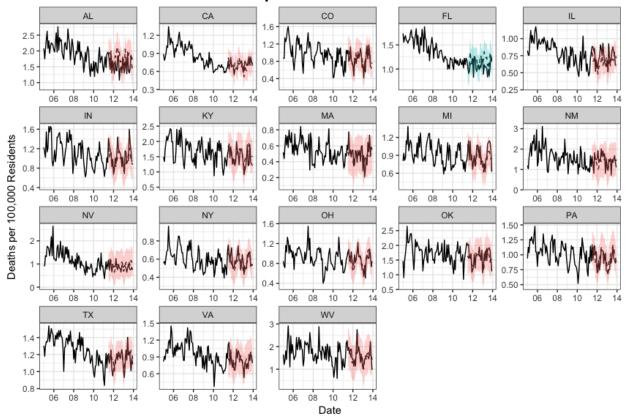
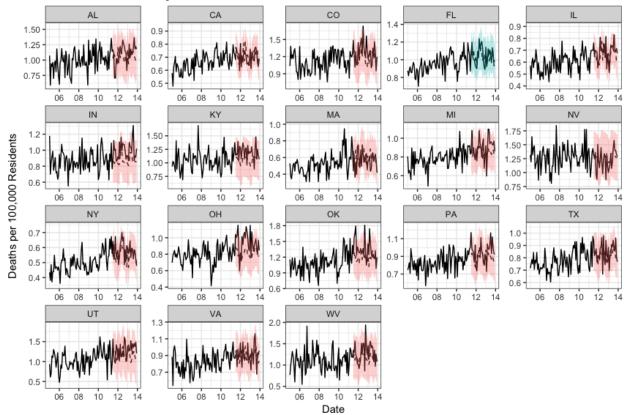
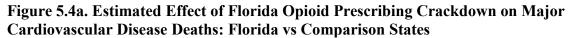


Figure 5.2a. Estimated Effect of Florida Opioid Prescribing Crackdown on Motor Vehicle Crash Deaths: Florida vs Comparison States

Figure 5.3a. Estimated Effect of Florida Opioid Prescribing Crackdown on Suicide Deaths: Florida vs Comparison States





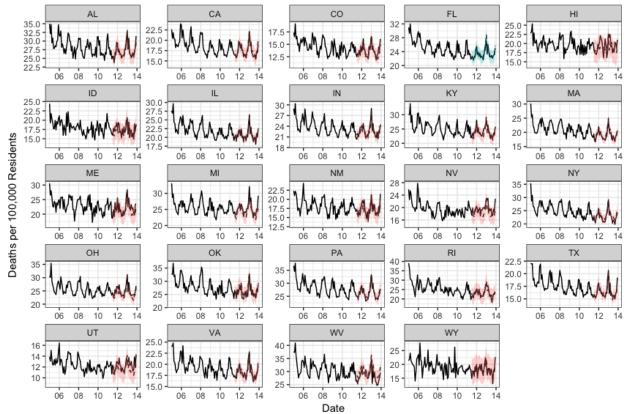
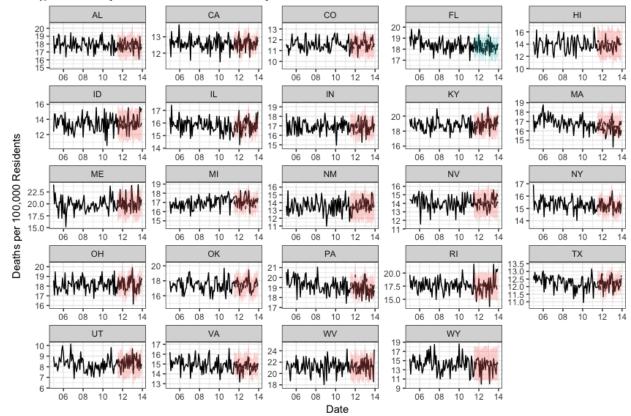


Figure 5.5a. Estimated Effect of Florida Opioid Prescribing Crackdown on Malignant Neoplasm: Florida vs Comparison States



CHAPTER 6. EFFECT OF FLORIDA'S OPIOID PRESCRIBING CRACKDOWN ON CHILD WELFARE INVOLVEMENT

6.0 Abstract

Background: Research shows increases in opioid misuse in a community are associated with concurrent increases in the number of children coming into contact with child protection. In 2011, Florida adopted a number of reforms that reduced problematic opioid prescribing and reduced overdose deaths. These reforms may have reduced child protection contact as well.

Methods: Quarterly rates of substantiated child physical abuse, child sexual abuse, neglect, and foster care entry were calculated for each state using administrative records. Trends in each outcome in Florida before and after July 2011 were examined. Counterfactual trends after July 2011 in the absence of reform are estimated using the observed behavior of 12 control states with Bayesian Structural Time-Series Models.

Results: Trends in all four maltreatment outcomes did not differ substantially from estimates of counterfactual trends in the absence of reforms.

Conclusion: We find no evidence that Florida's opioid prescribing reforms reduced substantiated maltreatment or foster care entry. Future research should explore which substance use policies or programs are effective at preventing child maltreatment and other collateral harms to children.

Keywords: Opioids, child welfare, interrupted time series

6.1 Introduction

6.1.1 The Opioid Epidemic and Child Welfare.

The United States is in the midst of a severe epidemic of opioid-related problems (Kolodny et al., 2015). As described in the introductory chapter, research suggests that opioid misuse by family, household, or community members is putting a growing number of children at risk for negative health or safety outcomes (Feder, Mojtabai, Musci, & Letourneau, 2018). As opioid related problems increase in a region, so do substantiated maltreatment cases (Ghertner, Baldwin, Crouse, Radel, & Waters, 2018), and intentional and unintentional injuries (Wolf, Ponicki, Kepple, & Gaidus, 2016). Increases in opioid prescriptions in a county have also been linked to increased rates of children placed in foster care (Quast, Storch, & Yampolskaya, 2018). Exposure to this type of adversity and trauma in childhood are believed to harmfully affect the development of important brain systems (Anda et al., 2006), and are subsequently associated with a wide range of adverse physical, behavioral, and mental health outcomes in adulthood, including many of the leading causes of death (Felitti et al., 1998). Taken together this research suggests that the harms of the present opioid include increased childhood exposure to chronic adversity and ensuing health problems.

In addition to these direct impacts on children, if a growing number of children are coming into contact with child protection systems because of the opioid epidemic, this could strain public child welfare systems capacity to respond to maltreatment writ large. Child welfare cases involving substance use tend to be complex and involve multiple risk factors. Parents with substance use problems often face other challenges such as domestic violence in the home, homelessness, or mental health problems (Patrick

& Schiff, 2017). As compared to other child welfare cases, parent substance use is overrepresented as a risk factor among child welfare cases that result in removal from the home (Barth, 2009). Among those children who are removed, cases involving family substance use appear to have longer average times to reunification (Brook, McDonald, Gregoire, Press, & Hindman, 2010; Vanderploeg et al., 2007), and may be less likely to end in reunification at all (Grella, Needell, Shi, & Hser, 2009). All of this suggests that, as the share of child welfare cases involving family substance use increases, so will strain on the child welfare system. Indeed, this is precisely what child welfare workers and administrators report in qualitative studies (Radel, Baldwin, Crouse, Ghertner, & Waters, 2018). If this strain grows too severe, it could impact the ability of child welfare agencies to adequately care for all children under their purview, both those whose cases involve family substance use and others.

6.1.2 Drug Policy and Child Welfare

If, as the evidence presented suggests, the United States' opioid epidemic is increasing risk to children's safety and health and straining the nation's child welfare system, then it is important to understand whether the public policy response to the opioid epidemic is meeting the needs of children and families. Although a number of promising practices and policies are described in the introductory chapter, most policies recommended by experts do not directly target children and families (Katz, 2018). This makes it important to examine broader drug control policies designed to prevent addiction in the first place. These policies do not directly target children and families, but to the extent that they effectively address some of the root causes of the opioid epidemic, may have ancillary benefits for children and families. This paper explores that possibility

by examining one such example – Florida's 2011 crackdown on irresponsible opioid prescribing practices.

6.1.3 Florida Reforms Targeting Opioid Prescribing

As described in Chapter 5, from the late 1990s until the end of the 2000s, opioid overdose deaths in Florida consistently exceeded the national average (National Institute on Drug Abuse, 2018). As a result, Florida adopted a number of reforms to try to reduce prescription drug-related mortality. These reforms included establishing a prescription drug monitoring program (PDMP), mandating that prescriptions of controlled substances be reported to and logged in the PDMP, and mandating that physicians who seek to prescribe an opioid to a patient first check the PDMP to review that patient's prescription history (Gau et al., 2017). Reforms also included defining "pain management clinics," requiring those clinics to register with the state, and establishing heightened standards for those clinics, including requiring physician ownership, prohibiting operation of onsite pharmacies, and requiring that opioid prescribing be accompanied by a medical exam and follow-up care (Gau et al., 2017). Following the adoption of these reforms, more than 500 of Florida's 900 independent pain management clinics closed (Gau et al., 2017). Opioid prescriptions fell as compared to other, similar states, with the largest reductions seen among doctors making the highest volume of prescriptions and patients receiving the highest volume of prescriptions (Rutkow et al., 2015). As shown both in Chapter 5, and by other authors, drug overdose deaths declined as compared to other similar states (Kennedy-Hendricks et al., 2016), with a steep decline in oxycodone overdoses in particular (Delcher, Wagenaar, Goldberger, Cook, & Maldonado-Molina, 2015).

6.1.4 Secondary Effects of Florida Policy on Children and Families

Taken together, these studies suggest that Florida's policy changes were, at least initially, effective at achieving their primary objective – reducing prescription drug overdose. (Overdose deaths in Florida have recently increased dramatically, probably because of a spike in deaths from illicit opioids like fentayl (National Institute on Drug Abuse, 2018)). In addition, in Chapter 5, we showed these policy changes may have had the secondary benefit of reducing motor vehicle crash deaths. Therefore, is important to identify if this reduction in opioid-related harms among adults had ancillary benefits by causing reductions in child maltreatment and child welfare contacts. On the one hand, we might expect a reduction in the opioid supply to lead to fewer parents developing an addiction, and consequently having better capacity to care for their children. On the other hand, interventions like the PDMP and pill mill laws might mostly benefit populations who do not have children, for example older adults with chronic pain, or may be inadequate to meet the needs of families using illicit drugs like heroin that are unaffected by prescription drug regulations.

This paper examines whether Florida's prescription drug monitoring program and "pill mill" law reduced the incidence of substantiated abuse and neglect and foster care placement relative to what would have occurred in Florida in the absence of these policies. Substantiated maltreatment in 12 other states, as well as substantiated maltreatment in Florida prior to prescribing reforms, are used to estimate what would have occurred in Florida had reforms not been adopted. The effects of policy change are examined in each of the three years following adoption of the policies.

6.2. Methods

6.2.1 Data

Data come from three sources:

- 1. The National Child Abuse and Neglect Data System (NCANDS) is a database of all reports of child maltreatment made to state child protection agencies. It is maintained by the US Department of Health and Human Services and is constructed from data submitted by each individual state. Each record corresponds to a report of maltreatment made against a child, and includes information on the nature, causes, and outcomes of the report, and the demographics of the victim and the perpetrator. Data from the 2002-2016 files were used in this analysis. Data are available upon request from the National Data Archive on Child Abuse and Neglect (Children's Bureau, n.d.-b).
- 2. The Adoption and Foster Care Analysis and Reporting System (AFCARS) is a database of all children placed in foster care by state child protection agencies. (Here, foster care refers to any out of home placement, including with kin, in a family foster home, in a group home, or in a residential treatment program.) It is maintained by the US Department of Health and Human Services and is constructed from data submitted by each individual state. Data from the 2002-2016 files were used in this analysis. Data are available upon request from the National Data Archive on Child Abuse and Neglect (Children's Bureau, n.d.-a).
- The U.S. Census maintains annual, intercensal estimates of the population of each state under the age of 18. These estimates can be found on the Census bureau's FTP site (https://www2.census.gov/programs-surveys/popest/).

Note that the analysis period for the study was Jan 1, 2003 to Dec 31, 2015, but some records corresponding to events in 2003 and 2015 were included in files for 2002 and 2016, respectively. These data were extracted from the 2002 and 2016 files.

6.2.2 Study Sample

The focus of this study is on the effect of Florida's PDMP and "pill mill" laws on child maltreatment. All maltreatment reports between Jan 1, 2003 and December 31, 2015 are included. Control states were selected based on two criteria. First, states had to report data to NCANDS and AFCARS in every year of the analysis. Second states had to have some type of PDMP law in place as early as 2002. This restriction was necessary because nearly every state that did not have a PDMP in 2002 had established one by the end of observation period – this could alter the association between maltreatment in the control states and maltreatment in Florida mid-study, violating an assumption of the method (see the "Assumptions" section). After exploratory analysis, Oklahoma and Utah, which met both criteria, were further excluded because of large fluctuations in substantiated abuse from year to year suggesting a possible reporting error or administrative change might have made the data unusable. In the neglect analysis (see the "Measures" section), Massachusetts and Illinois were also excluded for the same reason. Ultimately, thirteen control states were selected – California, Hawaii, Idaho, Illinois, Indiana, Kentucky, Massachusetts, New York, Pennsylvania, Rhode Island, Texas, Virginia, and West Virginia.

6.2.3 Measures

The unit of analysis is a state-quarter – the rate of the outcome in a quarter of a year (Q1, Jan-Mar; Q2, Apr-Jun; Q3, Jul-Sep; Q4, Oct-Dec) in a particular state.

Four outcome measures are examined for all state-quarters between Jan 1, 2002 and December 31, 2015:

6.2.3.1 Physical Abuse Rate. Computed by dividing the number of substantiated child abuse incidents reported in a state by the census estimate of the population under 18 in that state. Note that an incident is counted for each child affected; e.g., an investigation of one household with two substantiated abuse victims would contribute two incidents; e.g., an investigation of a household with three substantiated abuse victims, and then a second substantiated investigation of that same household one month later with three substantiated abuse victims, would contribute six incidents.

6.2.3.2 Sexual Abuse Rate. Computed similarly, but with sexual abuse cases.

6.2.3.3 Neglect Rate. Computed similarly, but with neglect cases.

6.2.3.4 Removal Rate. Computed by dividing the number of children placed in foster care in a state by the census estimate of the population under 18 in that state.

Florida's PDMP began operation at the beginning of 2011, but its "pill mill" went into effect on July 1, 2011 (Gau et al., 2017). Therefore, while some intervention effects may have begun slightly sooner, in this analysis, all quarters before July 1, 2011 are treated as the pre-intervention period, and all quarters July 1, 2011 and later are treated as post-intervention.

6.2.4 Analytic Approach

The approach is the same for all measures, so we refer generally to the "child welfare contact rate." The analytic approach is also very similar to Chapter 5 – refer to chapter 5 about details and assumptions of BSTS models.

The goal of the analysis is to determine how different Florida's child welfare contact rate would have been had it not adopted the opioid prescribing reforms described above (hereafter the "intervention"). Bayesian Structural Time Series (BSTS) models were used to forecast Florida's child welfare contact rate in the absence of the intervention. By taking the difference between our forecast and the observed rate, we estimate the effect of the intervention.

In this analysis, using BSTS, we average two simple models for Florida's behavior in the post-intervention period:

- 3. The first is an AR1 model, where Florida's child welfare contact rate is forecast iteratively as a function of its immediately prior value of the child welfare contact rate. (The decision to use an AR1 trend, rather than seasonal model as in Chapter 5, was based on exploratory analyses of predictive accuracy in control states.)
- 4. The second is a "spike-and-slab" linear regression model (Ishwaran & Rao, 2005), where Florida's child welfare contact rate in each quarter of the pre-intervention period is regressed on the contact rate in the comparison states. Spike-and-slab regression is a machine-learning approach similar to lasso or ridge regression that uses "shrinkage" to down-weight covariates that do less to improve predictive accuracy, reducing model variance and improving out-of-sample predictions as compared a simple linear regression (Ishwaran & Rao, 2005).

To all model parameters – regression coefficients, residual variances, and the autoregressive parameter – we assign so-called "non-informative" prior distributions, a common default choice in Bayesian analysis. These are consistent with the fact that we

have essentially no *a priori* knowledge about what these parameters should be. In addition, the spike-and-slab regression has a meta-parameter that must be chosen – the "expected model size" – which was set at 1.

To estimate the effect of the intervention, we fit a BSTS to forecast Florida's child welfare contact rate in the post-intervention period. For each MCMC iteration, for all quarters in the post-intervention period, we take the difference between our forecast and the observed value. This produces a full posterior distribution for the effect of the intervention at each post-intervention point. In addition, by converting rates into counts and taking the cumulative sum from the start of the intervention, we can estimate the cumulative change in the number of incidents by each time point as a result of the intervention for each MCMC iteration. Taking the mean and 0.025 and 0.975 quantiles of these posteriors give point estimates and 95% credible intervals for the effect of the intervention at each post-intervention point.

As before, to test the assumption that any divergence between predicted and observed rates are not due to model misspecification, we repeat the same analysis on each of the control states, and rank the estimated relative change in number of incidents in each state from least in magnitude to greatest in magnitude. Since control states did not adopt any intervention, estimated "intervention effects" should be zero in expectation, and much less negative than those observed in Florida. misspecification.

All models were estimating using the "BSTS" package in R (R Core Team, 2017; Scott, 2017).

6.3 Results

Trends in child protection involvement in Florida are shown in Table 1. In general, substantiated physical and sexual abuse and removals form the home all declined and substantiated neglect fluctuated over the study period.

Figure 1 shows the physical abuse, sexual abuse, neglect, and removal rates in Florida in each quarter of the 13-year period under observation. Superimposed on top are the BSTS-based forecast of these rates in the absence of the opioid crackdown. Florida's observed rate falls well within the 95% credible interval for the forecast rate at nearly all times for all measures of child maltreatment. Similarly, Figure 2 shows the estimated quarterly and cumulative change in the number of maltreatment cases of each type in Florida during the 2.5-year intervention period. Estimated changes are small and, for the most part, very much within the 95% credible interval of the counterfactual estimates.

Table 2 shows the estimated annual percent change in the child welfare contact rate, as well as cumulative change in the number of child welfare contacts, at three timepoints following the intervention. If Florida's pill mill law had reduced contact with child welfare, we would expect the intervention effect in Florida to be larger than most other states – instead, the magnitude of the intervention effect observed in Florida was 14th largest out of 14 states for physical abuse (i.e., the smallest effect), 9th out of 14 for sexual abuse, 7th out of 12 for neglect, and 9th out of 14 for removals. This suggests estimated intervention effects are no larger than would be expected based on chance. (Plots comparing Florida to other states are shown in Appendix A).

6.4. Discussion

Together, the evidence presented suggests Florida's opioid prescribing crackdown had no appreciable effect on child welfare contact in Florida. Our estimates of the effect

of this intervention were much smaller than the uncertainty in our estimates, and comparable to the "intervention effects" we estimated in states that did not actually implement any intervention. Since these laws had clear effects on problematic opioid prescribing and use (Kennedy-Hendricks et al., 2016; Rutkow et al., 2015), and opioidrelated problems in a region clearly linked to both child injury and substantiated maltreatment in that region (Ghertner et al., 2018; Wolf et al., 2016), it is worth considering why an effective opioid prescribing crackdown had no discernible effect on child maltreatment in Florida. At least three possibilities come to mind: First, our data come from child protection reports – these reports may be concentrated among families struggling with illicit opioids (which are likely unaffected by the policies we reviewed), rather than prescription drug misuse. This could be the case if other criminal justice involvement related to use of illegal drugs like heroin triggers child protection reports. Second, the opioid prescribing crackdown may disproportionately affect adults who are not currently caring for dependent children. This could be the case if much of the reduction in opioid prescribing was seen in older adults, who make a up disproportionate share of high-volume prescription opioid recipients and whose children may be grown (Kim, Hartung, Jacob, McCarty, & McConnell, 2016). Third, the impact of an opioid prescribing crackdown on child maltreatment might be more delayed than the immediate effect of the law on its proximal target – opioid prescribing and overdoses. This would be true if the harmful effects of opioid addiction on parenting grow more severe over the course of years. Since the uncertainty of our effect estimates is larger at times further from the intervention, if the law had benefits in later years, these would be exceedingly difficult to detect.

It should be noted that a recent working paper by Gihleb and colleagues examined a similar question – whether mandating PDMP use causes reductions in foster care entry (Gihleb, Giuntella, & Zhang, 2018). That paper also used data from AFCARS. However, it reached the opposite conclusion from this dissertation, finding that PDMP laws reduce rates of foster care entry. That study differs from the present study in a number of ways. Instead of examining the effect of a single state's intervention, that study attempts to find the average effect of adopting a PDMP law by using panel regression to compare trends in foster are entry before and after the adoption of PDMP laws. It is possible that, because of the particulars of its PDMP law, Florida's law did not have an impact in child maltreatment while other states' laws did. However, we prefer the approach adopted in this study - focusing on an intervention in a single state, and using flexible, semiparametric models to forecast counterfactual trends in that state. Focusing on a single state avoids the need to impose an equivalence between state laws that appear similar but can be quite different in their details or implementation. It also allows for more robust model checking, because any effects seen in the intervention state (Florida) can be compared to "effects" observed in control states – by contrast, in a panel regression where every state is included in the analytic model, there are no intuitive approaches to checking for inaccurate forecasts generated by model misspecification.

This study has a number of limitations. First, most child maltreatment is not reported to authorities. Child welfare contact is influenced by many policy decisions – for example, mandatory reporting laws, investigative practices, changes in the definition of a "substantiated" allegation, or social worker caseloads – other than the true rate of child maltreatment. Significant policy changes in any one of the control states might cause the

relationship between substantiated maltreatment in those states and Florida to change over time, whereas an assumption of our analysis is that, other than the effect of the intervention, this association is fixed in time. As noted, we partly address this assumption by comparing the estimate of the intervention effect in Florida to the intervention effects observed in control states. Second, we used a relatively short pre-intervention period – Q1 2003 through Q2 2011, 42 observations – to train our models.

6.5 Conclusion

We find no evidence that Florida's introduction of a PDMP and pill mill law reduced child maltreatment. However, we do present a novel method for precise estimation of intervention effects following policy change that we hope will be used by other child maltreatment researchers. Future research is needed to identify which states or policies, if any, are working to effectively reduce the harm to children being caused by the opioid epidemic. A comprehensive response to the opioid epidemic must include policies that go beyond prevention of the immediate overdose crisis and address the needs of struggling families and children, to prevent long term public health harms.

6.6. References

- Anda, R. F., Felitti, V. J., Bremner, J. D., Walker, J. D., Whitfield, C. H., Perry, B. D., ... Giles, W. H. (2006). The enduring effects of abuse and related adverse experiences in childhood. *European Archives of Psychiatry and Clinical Neuroscience*, 256(3), 174–186.
- Barth, R. P. (2009). Preventing child abuse and neglect with parent training: Evidence and opportunities. *The Future of Children*, *19*(2), 95–118.
- Brook, J., McDonald, T. P., Gregoire, T., Press, A., & Hindman, B. (2010). Parental Substance Abuse and Family Reunification. *Journal of Social Work Practice in the Addictions*, 10(4), 393–412. https://doi.org/10.1080/1533256X.2010.521078
- Children's Bureau. (n.d.-a). Adoption and Foster Care Analysis and Reporting System (AFCARS). Retrieved from https://www.ndacan.cornell.edu/
- Children's Bureau. (n.d.-b). National Child Abuse and Neglect Data System (NCANDS) Child Files. Retrieved from https://www.ndacan.cornell.edu/
- Delcher, C., Wagenaar, A. C., Goldberger, B. A., Cook, R. L., & Maldonado-Molina, M. M. (2015). Abrupt decline in oxycodone-caused mortality after implementation of Florida's Prescription Drug Monitoring Program. *Drug and Alcohol Dependence*, *150*, 63–68. https://doi.org/10.1016/j.drugalcdep.2015.02.010

Feder, K. A., Mojtabai, R., Musci, R. J., & Letourneau, E. J. (2018). U.S. adults with opioid use disorder living with children: Treatment use and barriers to care. *Journal of Substance Abuse Treatment*, 93, 31–37. https://doi.org/10.1016/j.jsat.2018.07.011

- Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V.,
 ... Marks, J. S. (1998). Relationship of childhood abuse and household
 dysfunction to many of the leading causes of death in adults: The Adverse
 Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine*, 14(4), 245–258.
- Gau, J. M., Moreto, W. D., Potter, R. H., Brooke, E. J., Florida, U. of C., & America, U.
 S. of. (2017). Non-medical Use of Prescription Drugs: Policy Change, Law
 Enforcement Activity, and Diversion Tactics. Department of Criminal Justice,
 University of Central Florida.
- Ghertner, R., Baldwin, M., Crouse, G., Radel, L., & Waters, A. (2018). The relationship between substance use indicators and child welfare caseloads. ASPE. Retrieved from

https://aspe.hhs.gov/system/files/pdf/258831/SubstanceUseCWCaseloads.pdf

- Gihleb, R., Giuntella, O., & Zhang, N. (2018). The Effects of Mandatory Prescription Drug Monitoring Programs on Foster Care Admissions.
- Grella, C. E., Needell, B., Shi, Y., & Hser, Y.-I. (2009). Do drug treatment services predict reunification outcomes of mothers and their children in child welfare? *Journal of Substance Abuse Treatment*, 36(3), 278–293.
- Ishwaran, H., & Rao, J. S. (2005). Spike and slab variable selection: frequentist and Bayesian strategies. *The Annals of Statistics*, *33*(2), 730–773.
- Katz, J. (2018, February 14). How a Police Chief, a Governor and a Sociologist WouldSpend \$100 Billion to Solve the Opioid Crisis The New York Times. RetrievedFebruary 19, 2018, from

https://www.nytimes.com/interactive/2018/02/14/upshot/opioid-crisis-solutions.html

- Kennedy-Hendricks, A., Richey, M., McGinty, E. E., Stuart, E. A., Barry, C. L., & Webster, D. W. (2016). Opioid Overdose Deaths and Florida's Crackdown on Pill Mills. *American Journal of Public Health*, *106*(2), 291–297. https://doi.org/10.2105/AJPH.2015.302953
- Kim, H., Hartung, D., Jacob, L., McCarty, D., & McConnell, K. J. (2016). The Concentration of Opioid Prescriptions by Providers and Patients in the Oregon Medicaid Program. *Psychiatric Services (Washington, D.C.)*, 67(4), 397–404. https://doi.org/10.1176/appi.ps.201500116
- Kolodny, A., Courtwright, D. T., Hwang, C. S., Kreiner, P., Eadie, J. L., Clark, T. W., & Alexander, G. C. (2015). The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. *Annual Review of Public Health*, 36, 559– 574.
- National Institute on Drug Abuse. (2018, February 28). Florida Opioid Summary. Retrieved June 29, 2018, from https://www.drugabuse.gov/drugsabuse/opioids/opioid-summaries-by-state/florida-opioid-summary
- NPO Staff. (2018, July). LawAtlas Policy Surveillance Report, Query Report on Dataset: Query where At least one of these selections apply - Does this state have legislation authorizing access by professionals to a PDMP system? Retrieved from lawaltas.org/preview?dataset=prescription-monitoring-program-laws-1408223332

- Patrick, S. W., & Schiff, D. M. (2017). A Public Health Response to Opioid Use in Pregnancy. *Pediatrics*, e20164070.
- Quast, T., Storch, E. A., & Yampolskaya, S. (2018). Opioid Prescription Rates And Child Removals: Evidence From Florida. *Health Affairs*, 37(1), 134–139. https://doi.org/10.1377/hlthaff.2017.1023
- R Core Team. (2017). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from https://www.Rproject.org/
- Radel, L., Baldwin, M., Crouse, G., Ghertner, R., & Waters, A. (2018). Substance use, the opioid epidemic, and the child welfare system: Key Findings from a Mixed Methods Study. ASPE. Retrieved from https://aspe.hhs.gov/system/files/pdf/258836/SubstanceUseChildWelfareOvervie w.pdf
- Rutkow, L., Chang, H.-Y., Daubresse, M., Webster, D. W., Stuart, E. A., & Alexander,
 G. C. (2015). Effect of Florida's Prescription Drug Monitoring Program and Pill
 Mill Laws on Opioid Prescribing and Use. *JAMA Internal Medicine*, *175*(10),
 1642. https://doi.org/10.1001/jamainternmed.2015.3931
- Scott, S. L. (2017, July 11). Fitting Bayesian structural time series with the bsts R package. Retrieved from http://www.unofficialgoogledatascience.com/2017/07/fitting-bayesian-structuraltime-series.html
- Vanderploeg, J. J., Connell, C. M., Caron, C., Saunders, L., Katz, K. H., & Tebes, J. K. (2007). The impact of parental alcohol or drug removals on foster care placement

experiences: A matched comparison group study. *Child Maltreatment*, *12*(2), 125–136. https://doi.org/10.1177/1077559507299292

Wolf, J. P., Ponicki, W. R., Kepple, N. J., & Gaidus, A. (2016). Are community level prescription opioid overdoses associated with child harm? A spatial analysis of California zip codes, 2001–2011. Drug and Alcohol Dependence, 166, 202–208.

6.7 Exhibits

 Table 6.1. Quarterly Counts and Rates of Child Welfare Contact Before and After Florida's Opioid Prescribing Crackdown

 Beginning July 2011

Date	Physical Abuse Count (Rate)	Sexual Abuse Count (Rate)	Neglect Count (Rate)	Removals Count (Rate)
January - March, 2003	1678 (4.4)	616 (1.6)	4136 (10.8)	5034 (13.2)
April - Jun, 2011	1332 (3.3)	648 (1.6)	7775 (19.5)	4198 (10.5)
October - December, 2014	1083 (2.7)	563 (1.4)	5789 (14.3)	4038 (10)

Note: Rate is events per 10,000 children during the three-month period.

 Table 6.2. Estimated Percent Change in Child Welfare Contact following Florida's Opioid Prescribing Crackdown, July 2011-July 2014

	July - Sep, 2011	July - Sep, 2012	July - Sep, 2013	July - Sep, 2014
Physical Abuse				
Annual Percent Change	1.9% (-18.5% to 31.2%)	-1.1% (-26.1% to 42.4%)	-6.8% (-33.3% to 42.8%)	-23.3% (-45.3% to 26.8%)
Cumulative Percent Change	1.9% (-18.5% to 31.2%)	6.3% (-10.8% to 31.7%)	4.8% (-13.3% to 34.6%)	-0.4% (-18.6% to 32.4%)
Sexual Abuse				
Annual Percent Change	4.9% (-13.8% to 30.9%)	16.9% (-6.9% to 49%)	2.2% (-20.1% to 32.7%)	13.1% (-16.5% to 78.2%)
Cumulative Percent Change	4.9% (-13.8% to 30.9%)	5% (-10.4% to 21.4%)	4.4% (-11.4% to 20.7%)	5.4% (-11.4% to 23.6%)
Neglect				
Annual Percent Change	7.6% (-8.7% to 29.5%)	-2.9% (-28.3% to 38.8%)	-6.5% (-36.5% to 48.1%)	-17.9% (-47% to 41.6%)
Cumulative Percent Change	7.6% (-8.7% to 29.5%)	3.4% (-16.1% to 30.2%)	-1.3% (-23.7% to 30.4%)	-5% (-29% to 30.9%)
Foster Care Entry				
Annual Percent Change	7.6% (-8.7% to 29.5%)	-2.9% (-28.3% to 38.8%)	-6.5% (-36.5% to 48.1%)	-17.9% (-47% to 41.6%)
Cumulative Percent Change	7.6% (-8.7% to 29.5%)	3.4% (-16.1% to 30.2%)	-1.3% (-23.7% to 30.4%)	-5% (-29% to 30.9%)

Effects presented as: Estimate (95% Credible Interval)

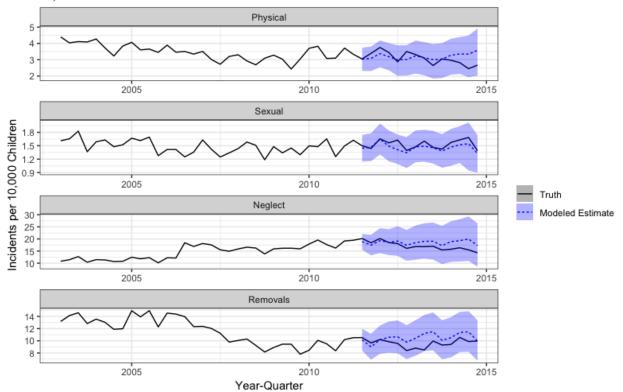


Figure 6.1. Rates of True and Model-Estimated Substantiated Maltreatment in Florida, 2003-2014.

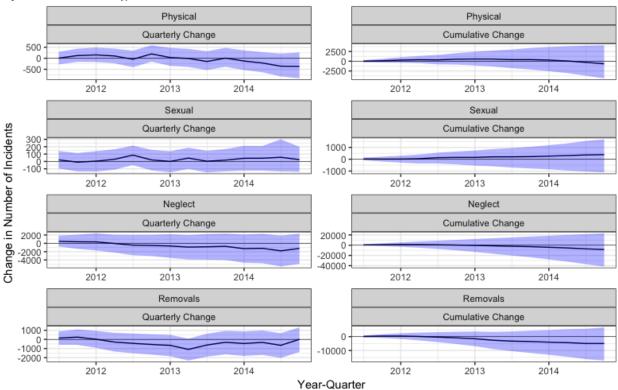


Figure 6.2. Estimated Change in Child Maltreatment Incidents following Florida Opioid Prescribing Crackdown

6.8 Appendix Exhibits

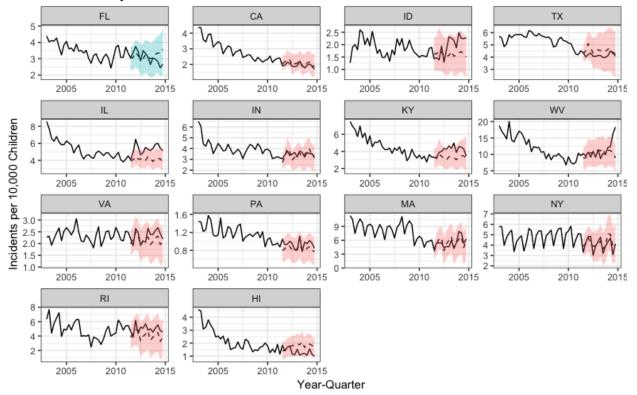


Figure 6.1a. Estimated Effect of Florida Opioid Prescribing Crackdown on Substantiated Physical Abuse: Florida vs Control States

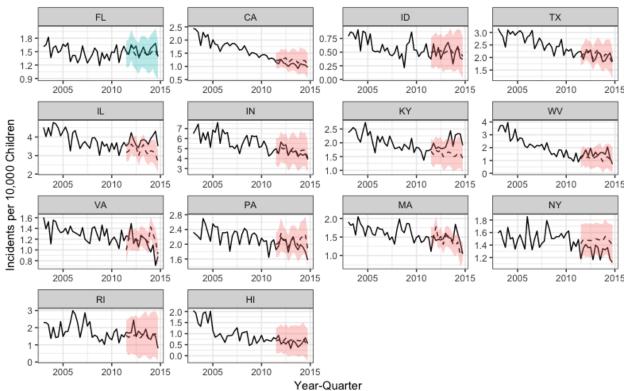


Figure 6.2a. Estimated Effect of Florida Opioid Prescribing Crackdown on Substantiated Sexual Abuse: Florida vs Control States

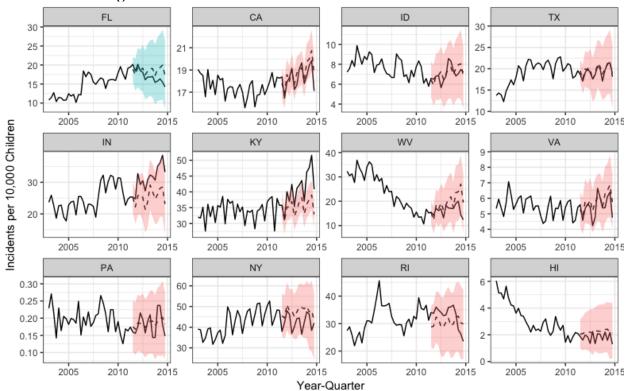


Figure 6.3a. Estimated Effect of Florida Opioid Prescribing Crackdown on Substantiated Neglect: Florida vs Control States

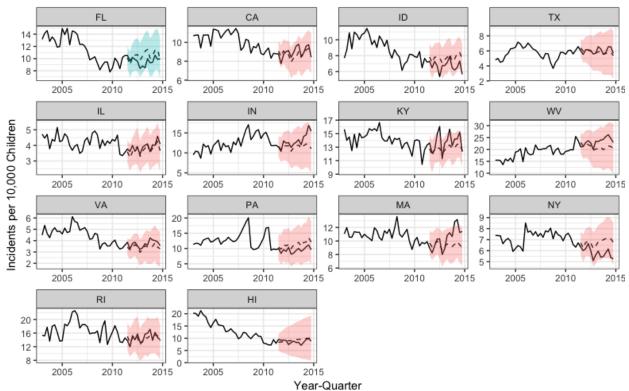


Figure 6.4a. Estimated Effect of Florida Opioid Prescribing Crackdown on Removals for Foster Care: Florida vs Control States

CHAPTER 7. CONCLUSION AND RECOMMENDATIONS

7.1 Conclusion

This dissertation examines the United States opioid epidemic's effect on children. It looks at both the childhood experiences of adults currently struggling with opioid misuse, the experiences of children growing in households where an adult has an opioid use disorder, and the impact of opioid prescription policies on child welfare involvement. This program of research is in contrast to most research on the opioid epidemic, which has focused on preventing the immediate crisis of adult overdoses. While overdose prevention is an urgent and worthy goal, as the research presented here should make clear, there is also an urgent public health need to both understand the pediatric causes of opioid misuse and address the pediatric consequences of parents' opioid misuse.

This dissertation addresses a number of novel questions that contribute to our understanding of both the pediatric causes of opioid misuse and pediatric consequences of parents' opioid misuse:

7.1.1 Aim 1

7.1.1.1 Goal. Make the first estimate of the number of children growing up in a household where an adult has an opioid use disorder. Examine the prevalence of substance use treatment utilization among the adults in these households. Examine if these adults living with children face unique barriers to care that are less common among their counterparts among children.

7.1.1.2 Findings. There are about 820,000 adults with an opioid use disorder living with at least one child. Of these, 28% reported receiving any substance use treatment in the past year, a rate comparable to adults not living with a child (30%). Among adults reporting unmet treatment need, adults who lived with a child were more

likely than adults who did not live with a child to report that 1) access barriers like not being able to find the right kind of program and 2) stigma from acquaintances or colleagues kept them from receiving care.

7.1.1.3 Conclusion. There are many children growing up in a household with an adult who has an opioid use disorder, and most of these adults are not receiving any treatment. While treatment use is similar to adults living without children, expanding programs that specifically accommodate the needs of adults living with children and using public awareness campaigns to address the stigma of opioid use disorder may be important to helping adults with children access needed treatment.

7.1.2 Aim 2

7.1.2.1 Goal. Explores heterogeneity in common trajectories of heroin use over the life course of people who have injected drugs. Examine if childhood adversity predicts a more severe trajectory of substance use.

7.1.2.2 Results. While, on average, the probability of heroin and cocaine use declines with age, there is substantial heterogeneity in trajectories of heroin and cocaine use. Some common subtypes of heroin use are people whose heroin use declines sharply to zero or near-zero without relapse; people who have a fairly constant, moderate probability of using heroin that continues for years; and people who relapse to very high probability of use late in life. Further, adverse childhood experiences may explain some of this heterogeneity – reporting more than five adverse childhood experiences is associated with substantially elevated risk for sustained heroin use into middle-to-late adulthood, as compared to people who report fewer than five adverse experience.

7.1.2.3 Conclusions. A history of childhood adversity is associated with continuing heroin use into older adulthood, even as peers who used heroin but experienced less adversity have stopped using. This suggests treatment programs that address the lasting psychological and physical consequences of childhood trauma may be important to meeting the needs of people whose heroin use is chronic and sustained into late adulthood.

7.1.3 Aim 3

7.1.3.1 Goal. Given past research showing parent opioid misuse is associated with maladaptive parenting and child welfare involvement, test whether a Florida state policy to reduce opioid misuse had the ancillary benefit of preventing contact with the child welfare system, and develop methods for evaluating similar policies.

7.1.3.2 Results. The policy examined was Florida's reform that cracked down on "pill mills" and required physicians to check a prescription drug monitoring program (PDMP) before prescribing an opioid. In a preliminary analysis, Bayesian Structural Time Series (BSTS) models were used to show overdose deaths declined after the introduction of these reforms but suicides did not. In the main analysis, no effect was seen on the policy on substantiated incidents of child abuse or neglect, or on rates of foster care entry.

7.1.3.3 Conclusion. Florida's pill mill and PDMP are examples of initiatives that effectively reduced adult overdose deaths, but do not appear to have reduced any potential collateral consequences of the opioid epidemic for children. BSTS models are a potentially useful tool for evaluating other opioid-related policies, to test for both intended effects on overdose death, and secondary effects on child welfare contact.

7.2 Recommendations.

In combination, these results lend themselves to four recommendations:

1. Leverage new federal funding opportunities for maltreatment prevention to improve collaboration between child welfare, behavioral health, and justice systems. The need for improved collaboration between these three systems is made clear both by the introductory literature review, and by the novel finding presented here that nearly 1 million adults with an opioid use disorder are living with child, but fewer than a third receive any treatment. Collaboration between these three systems is required to both increase the number of parents with opioid use disorder receiving evidence-based treatment, and meet the needs of children while parents are in treatment. For years, these treatment programs have been supported on a case-by-case basis using demonstration funding from the Children's Bureau's "Regional Partnership Grant" program. These demonstration programs provide substantial experience that can inform other sites and reigions that want to improve inter-agency collaboration around family substance use (Stedt & DeCerchio, 2016). Further, beginning in 2019, State costs associated with timelimited substance use, mental health, and parent training services provided to families with a child at risk of entering foster care will, for the first time, be partially reimbursed by the federal government (Feder, Letourneau, & Brook, 2018). This new funding offers an excellent opportunity for states that have not received regional partnership grants to build on the lesson of those grants and improve inter-agency collaboration for families with substance use problems.

2. Prioritize medication-assisted treatment for child welfare involved families, and complement this treatment with specialized programs that target the

needs of pregnant women and parents. This second recommendation is the major positive outcome that should result from the first. Past research has shown that medication-assisted treatments are the preferred treatments for opioid use disorder generally, and for pregnant and child welfare involved parents specifically (Hall, Wilfong, Huebner, Posze, & Willauer, 2016; Patrick & Schiff, 2017). The research in this dissertation shows that, despite these benefits, most adults with an opioid use disorder who live with a child do not receive any treatment at all. Further, this dissertation finds that adults with children are more likely to report they cannot find the kind of program that they are looking for than adults without children. This strongly suggests that improved collaboration between child welfare and substance use treatment agencies should include prioritizing medication-assisted treatment slots for parents, for whom the benefits of treatment are double. Further, simply making treatment available is not enough – it is likely that the programs parents need include child care and specialty services like parent training or programs for domestic violence victims.

3. Incorporate trauma-informed practices into substance use disorder treatment, particularly for chronic or relapsing users. This dissertation shows that adults who inject drugs often have a significant history of childhood adversity. Further, it shows that among adults who are already using heroin or cocaine, having experienced high levels of trauma or adversity in childhood is associated with continuing to use both drugs into late adulthood, even as peers with a similar history of drug use stop but less childhood adversity using. While we could only study heroin in this paper, there is no reason to think the association of childhood adversity with misuse of other opioid drugs would be dramatically different. This is valuable information that can should inform the

development of new treatments for the most persistent opioid users. In particular, it should motivate the adoption of trauma-informed practice in substance use treatment programs – the high rates of trauma observed in this study and others suggest trauma-informed practice needs to be the norm, not just a component of some specialized programming.

4. Rapidly evaluating state opioid policies for secondary effects like changes in suicide or child welfare involvement. Finally, this dissertation offers discouraging evidence that some policies that are effective at reducing adult overdose deaths are not effective at reducing other ancillary harms to children that have been associated with the opioid epidemic, like child abuse and foster care involvement. However, it also presents a model for how to evaluate opioid-related policies for their effects on children. This should be a priority of future research. Over the next several years, states will undoubtedly introduce dozens of new policies in an attempt to combat opioid-related harms. It will be important to rigorously test not only whether these policies benefit adults with opioid use disorder, but also whether they effectively protect children.

Adoption of these recommendations, and continuing the child-focused research introduced in this dissertation, can both help remediate the harms of this epidemic and prevent a future one.

7.3 References

- Feder, K. A., Letourneau, E. J., & Brook, J. (2018). Children in the Opioid Epidemic: Addressing the Next Generation's Public Health Crisis. *Pediatrics*, e20181656. https://doi.org/10.1542/peds.2018-1656
- Hall, M. T., Wilfong, J., Huebner, R. A., Posze, L., & Willauer, T. (2016). Medication-Assisted Treatment Improves Child Permanency Outcomes for Opioid-Using Families in the Child Welfare System. *Journal of Substance Abuse Treatment*, *71*, 63–67.
- Patrick, S. W., & Schiff, D. M. (2017). A Public Health Response to Opioid Use in Pregnancy. *Pediatrics*, e20164070.
- Stedt, E. V., & DeCerchio, K. (2016, August). Regional Partnership Grants Collaborative Approaches: Lessons Learned from the RPG Program. Presented at the Child Welfare League of America National Conference, Orange County, California, USA. Retrieved from https://www.cwla.org/wpcontent/uploads/2016/09/D3_Workshop_RPG_Final.pdf

BIBLIOGRAPHY

- Abadie, A., Diamond, A., & Hainmueller, J. (2010). Synthetic control methods for comparative case studies: Estimating the effect of California's tobacco control program. *Journal of the American Statistical Association*, 105(490), 493–505.
- Ahrnsbrak, R., Bose, J., Hedden, S. L., Lipari, R. N., & Park-Lee, E. (2017). Key substance use and mental health indicators in the United States: Results from the 2016 National Survey on Drug Use and Health. *Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration: Rockville, MD, USA.*
- Alexander, G. C., Frattaroli, S., & Gielen, A. C. (2015). The Prescription Opioid Epidemic: An Evidence-Based Approach. Johns Hopkins Bloomberg School of Public Health,© 2015.
- Ali, M. M., Teich, J. L., & Mutter, R. (2015). The role of perceived need and health insurance in substance use treatment: implications for the Affordable Care Act. *Journal of Substance Abuse Treatment*, 54, 14–20.
- Altilio, T., Brennan, M., Dahl, J., Edwards, A., Fouladbakhsh, J., & Keefe, F. (2007).
 Treatment Options: A Guide for People Living with Pain. *Baltimore, MD: American Pain Foundation*.
- Anda, R. F., Brown, D. W., Felitti, V. J., Dube, S. R., & Giles, W. H. (2008). Adverse childhood experiences and prescription drug use in a cohort study of adult HMO patients. *BMC Public Health*, 8(1), 198.
- Anda, R. F., Felitti, V. J., Bremner, J. D., Walker, J. D., Whitfield, C. H., Perry, B. D., ...Giles, W. H. (2006). The enduring effects of abuse and related adverse

experiences in childhood. *European Archives of Psychiatry and Clinical Neuroscience*, 256(3), 174–186.

Andersen, R. M. (1995). Revisiting the behavioral model and access to medical care: does it matter? *Journal of Health and Social Behavior*, 1–10.

Associated Press. (2018, November 29). CDC says life expectancy down as more Americans die younger due to suicide and drug overdose. Retrieved December 6, 2018, from https://www.cbsnews.com/news/cdc-us-life-expectancy-decliningdue-largely-to-drug-overdose-and-suicides/

- Avinun, R., & Knafo, A. (2014). Parenting as a reaction evoked by children's genotype:
 A meta-analysis of children-as-twins studies. *Personality and Social Psychology Review*, 18(1), 87–102.
- Baglivio, M. T., Epps, N., Swartz, K., Huq, M. S., Sheer, A., & Hardt, N. S. (2014). The prevalence of adverse childhood experiences (ACE) in the lives of juvenile offenders. *Journal of Juvenile Justice*, 3(2).
- Barnard, M., & McKeganey, N. (2004). The impact of parental problem drug use on children: what is the problem and what can be done to help? *Addiction*, 99(5), 552–559.
- Barth, R. P. (2009). Preventing child abuse and neglect with parent training: Evidence and opportunities. *The Future of Children*, *19*(2), 95–118.
- Bell, M. L., Kenward, M. G., Fairclough, D. L., & Horton, N. J. (2013). Differential dropout and bias in randomised controlled trials: when it matters and when it may not. *The BMJ*, 346. https://doi.org/10.1136/bmj.e8668

- Bernal, J. L., Cummins, S., & Gasparrini, A. (2017). Interrupted time series regression for the evaluation of public health interventions: a tutorial. *International Journal* of Epidemiology, 46(1), 348–355. https://doi.org/10.1093/ije/dyw098
- Brodersen, K. H., Gallusser, F., Koehler, J., Remy, N., & Scott, S. L. (2015). Inferring causal impact using Bayesian structural time-series models. Retrieved from https://research.google.com/pubs/pub41854.html
- Brook, J., McDonald, T. P., Gregoire, T., Press, A., & Hindman, B. (2010). Parental Substance Abuse and Family Reunification. *Journal of Social Work Practice in the Addictions*, 10(4), 393–412. https://doi.org/10.1080/1533256X.2010.521078
- Bruhn, C. A. W., Hetterich, S., Schuck-Paim, C., Kürüm, E., Taylor, R. J., Lustig, R., ... Weinberger, D. M. (2017). Estimating the population-level impact of vaccines using synthetic controls. *Proceedings of the National Academy of Sciences*, *114*(7), 1524–1529. https://doi.org/10.1073/pnas.1612833114

Buchanich, J. M., Balmert, L. C., Williams, K. E., & Burke, D. S. (2018). The Effect of Incomplete Death Certificates on Estimates of Unintentional Opioid-Related Overdose Deaths in the United States, 1999-2015. *Public Health Reports (Washington, D.C.: 1974)*, *133*(4), 423–431. https://doi.org/10.1177/0033354918774330

- Buerkner, P.-C. (2016). brms: An R package for Bayesian multilevel models using Stan. Journal of Statistical Software.
- Card, D., & Krueger, A. B. (1994). Minimum Wages and Employment: A Case Study of the Fast-Food Industry in New Jersey and Pennsylvania. *The American Economic Review*, 84(4), 772–793.

- Carissimo, J. (2016, September 14). Four-year-old boy pictured in car with parents overdosed on heroin finds new home. Retrieved March 15, 2018, from http://www.independent.co.uk/news/world/americas/heroin-overdose-parents-carphoto-boy-finds-new-home-ohio-a7307391.html
- Carpenter, B., Gelman, A., Hoffman, M. D., Lee, D., Goodrich, B., Betancourt, M., ... Riddell, A. (2017). Stan: A probabilistic programming language. *Journal of Statistical Software*, 76(1).
- Celeux, G., & Soromenho, G. (1996). An entropy criterion for assessing the number of clusters in a mixture model. *Journal of Classification*, *13*(2), 195–212.
- Center for Behavioral Health and Quality Statistics. (2015). National Survey on Drug Use and Health: 2014 and 2015 Redesign Changes. Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data/sites/default/files/NSDUH-RedesignChanges-2015.pdf
- Centers for Disease Control and Prevention, National Center for Health Statistics. (2017). *Underlying Cause of Death 1999-2016 on CDC WONDER Online Database, released December, 2017. Data are from the Multiple Cause of Death Files, 1999-2016, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program.* Retrieved from http://wonder.cdc.gov/ucd-icd10.html
- Children's Bureau. (n.d.-a). Adoption and Foster Care Analysis and Reporting System (AFCARS). Retrieved from https://www.ndacan.cornell.edu/

- Children's Bureau. (n.d.-b). National Child Abuse and Neglect Data System (NCANDS) Child Files. Retrieved from https://www.ndacan.cornell.edu/
- Christie, G. C., Baker, C. G. C., Cooper, G. R., Kennedy, C. P. J., Madras, B., & Bondi,F. A. G. P. (n.d.). THE PRESIDENT'S COMMISSION ON COMBATINGDRUG ADDICTION AND THE OPIOID CRISIS.
- Connery, H. S. (2015). Medication-assisted treatment of opioid use disorder: review of the evidence and future directions. *Harvard Review of Psychiatry*, *23*(2), 63–75.
- Conroy, E., Degenhardt, L., Mattick, R. P., & Nelson, E. C. (2009). Child maltreatment as a risk factor for opioid dependence: Comparison of family characteristics and type and severity of child maltreatment with a matched control group. *Child Abuse & Neglect*, 33(6), 343–352.
- Darke, S. (2013). Pathways to heroin dependence: time to re-appraise self-medication. *Addiction*, *108*(4), 659–667.
- Davis, D. A., Luecken, L. J., & Zautra, A. J. (2005). Are reports of childhood abuse related to the experience of chronic pain in adulthood?: a meta-analytic review of the literature. *The Clinical Journal of Pain*, 21(5), 398–405.
- Dawe, S., & Harnett, P. (2007). Reducing potential for child abuse among methadonemaintained parents: Results from a randomized controlled trial. *Journal of Substance Abuse Treatment*, 32(4), 381–390.
- Delcher, C., Wagenaar, A. C., Goldberger, B. A., Cook, R. L., & Maldonado-Molina, M. M. (2015). Abrupt decline in oxycodone-caused mortality after implementation of Florida's Prescription Drug Monitoring Program. *Drug and Alcohol Dependence*, *150*, 63–68. https://doi.org/10.1016/j.drugalcdep.2015.02.010

Demidenko, M. I., Dobscha, S. K., Morasco, B. J., Meath, T. H. A., Ilgen, M. A., & Lovejoy, T. I. (2017). Suicidal ideation and suicidal self-directed violence following clinician-initiated prescription opioid discontinuation among long-term opioid users. *General Hospital Psychiatry*, 47, 29–35. https://doi.org/10.1016/j.genhosppsych.2017.04.011

Diaz, N., Horton, E. G., & Malloy, T. (2014). Attachment Style, Spirituality, and
Depressive Symptoms Among Individuals in Substance Abuse Treatment. *Journal of Social Service Research*, 40(3), 313–324.
https://doi.org/10.1080/01488376.2014.896851

- Doleac, J. L., & Mukherjee, A. (2018). *The Moral Hazard of Lifesaving Innovations: Naloxone Access, Opioid Abuse, and Crime* (SSRN Scholarly Paper No. ID 3135264). Rochester, NY: Social Science Research Network. Retrieved from https://papers.ssrn.com/abstract=3135264
- Dowell, D., Haegerich, T. M., & Chou, R. (2016). CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR. Recommendations and Reports, 65. https://doi.org/10.15585/mmwr.rr6501e1er
- Dube, S. R., Felitti, V. J., Dong, M., Chapman, D. P., Giles, W. H., & Anda, R. F. (2003).
 Childhood abuse, neglect, and household dysfunction and the risk of illicit drug use: the adverse childhood experiences study. *Pediatrics*, *111*(3), 564–572.
- Dubois, S., Bédard, M., & Weaver, B. (2010). The association between opioid analgesics and unsafe driving actions preceding fatal crashes. *Accident Analysis & Prevention*, 42(1), 30–37. https://doi.org/10.1016/j.aap.2009.06.030

- Enoch, M.-A. (2011). The role of early life stress as a predictor for alcohol and drug dependence. *Psychopharmacology*, *214*(1), 17–31.
- European Monitoring Center for Drugs and Drug Addiction. (2012). *Pregnancy, Childcare and the Family: Key Issues for Europe's Response to Drugs*. Retrieved from Publications Office of the European Union website: http://www.emcdda.europa.eu/system/files/publications/671/TDSI12001ENC_39 6469.PDF
- Feder, K. A., & Krawczyk, N. (2017, August). Four facts every journalist should know when covering the opioid epidemic. *Columbia Journalism Review*. Retrieved from https://www.cjr.org/united_states_project/opioid-journalist-advice.php
- Feder, K. A., Letourneau, E. J., & Brook, J. (2018). Children in the Opioid Epidemic: Addressing the Next Generation's Public Health Crisis. *Pediatrics*, e20181656. https://doi.org/10.1542/peds.2018-1656
- Feder, K. A., Mojtabai, R., Krawczyk, N., Young, A. S., Kealhofer, M., Tormohlen, K. N., & Crum, R. M. (2017). Trends in insurance coverage and treatment among persons with opioid use disorders following the Affordable Care Act. *Drug and Alcohol Dependence*, 179, 271–274.
- Feder, K. A., Mojtabai, R., Musci, R. J., & Letourneau, E. J. (2018). U.S. adults with opioid use disorder living with children: Treatment use and barriers to care. *Journal of Substance Abuse Treatment*, 93, 31–37. https://doi.org/10.1016/j.jsat.2018.07.011
- Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V.,... Marks, J. S. (1998). Relationship of childhood abuse and household

dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine*, *14*(4), 245–258.

- Finkelhor, D., Ormrod, R., Turner, H., & Hamby, S. L. (2005). The victimization of children and youth: a comprehensive, national survey. *Child Maltreatment*, 10(1), 5–25. https://doi.org/10.1177/1077559504271287
- Finkelhor, D., Shattuck, A., Turner, H., & Hamby, S. (2015). A revised inventory of adverse childhood experiences. *Child Abuse & Neglect*, 48, 13–21.
- Fishbain, D. A., Cutler, R. B., Rosomoff, H. L., & Rosomoff, R. S. (2002). Can Patients Taking Opioids Drive Safely?? *Journal of Pain & Palliative Care Pharmacotherapy*, 16(1), 9–28. https://doi.org/10.1080/J354v16n01_03
- Frank, R. G., Humphreys, K., & Pollack, H. A. (2018, March 19). Does Naloxone
 Availability Increase Opioid Abuse? The Case for Skepticism. Retrieved April 23, 2018, from
 https://www.healthaffairs.org/do/10.1377/hblog20180316.599095/full/#.Wq_oPlJ
 aD2c.twitter
- Gau, J. M., Moreto, W. D., Potter, R. H., Brooke, E. J., Florida, U. of C., & America, U.
 S. of. (2017). Non-medical Use of Prescription Drugs: Policy Change, Law
 Enforcement Activity, and Diversion Tactics. Department of Criminal Justice,
 University of Central Florida.
- Genberg, B. L., Gange, S. J., Go, V. F., Celentano, D. D., Kirk, G. D., & Mehta, S. H.
 (2011). Trajectories of injection drug use over 20 years (1988–2008) in
 Baltimore, Maryland. *American Journal of Epidemiology*, 173(7), 829–836.

Ghertner, R., Baldwin, M., Crouse, G., Radel, L., & Waters, A. (2018). The relationship between substance use indicators and child welfare caseloads. ASPE. Retrieved from

https://aspe.hhs.gov/system/files/pdf/258831/SubstanceUseCWCaseloads.pdf

- Gihleb, R., Giuntella, O., & Zhang, N. (2018). The Effects of Mandatory Prescription Drug Monitoring Programs on Foster Care Admissions.
- Governors Highway Safety Assocation. (2018). Drug Impaired Driving: Marijuana and Opioids Raise Critical Issues for States. Retrieved from https://www.insurancejournal.com/app/uploads/2018/05/GHSA_DrugImpairedDri ving_FINAL-1.pdf
- Grant, T. M., Ernst, C. C., Streissguth, A., & Stark, K. (2005). Preventing alcohol and drug exposed births in Washington State: Intervention findings from three Parent-Child Assistance Program sites. *The American Journal of Drug and Alcohol Abuse*, 31(3), 471–490.
- Greenfield, S. F., Brooks, A. J., Gordon, S. M., Green, C. A., Kropp, F., McHugh, R. K.,
 ... Miele, G. M. (2007). Substance abuse treatment entry, retention, and outcome in women: A review of the literature. *Drug and Alcohol Dependence*, 86(1), 1–21.
- Grella, C. E., Needell, B., Shi, Y., & Hser, Y.-I. (2009). Do drug treatment services predict reunification outcomes of mothers and their children in child welfare? *Journal of Substance Abuse Treatment*, 36(3), 278–293.
- Haastrup, S., & Jepsen, P. W. (1988). Eleven year follow-up of 300 young opioid addicts. *Acta Psychiatrica Scandinavica*, 77(1), 22–26.

- Haggerty, K. P., Skinner, M., Fleming, C. B., Gainey, R. R., & Catalano, R. F. (2008).
 Long-term effects of the Focus on Families project on substance use disorders among children of parents in methadone treatment. *Addiction*, 103(12).
- Hall, M. T., Wilfong, J., Huebner, R. A., Posze, L., & Willauer, T. (2016). Medication-Assisted Treatment Improves Child Permanency Outcomes for Opioid-Using Families in the Child Welfare System. *Journal of Substance Abuse Treatment*, *71*, 63–67.
- Healthcare Cost and Utilization Project (HCUP). (2018). HCUP Fast Stats. Rockville,
 MD: Agency for Healthcare Research and Quality. Retrieved from
 https://www.hcup-us.ahrq.gov/faststats/OpioidUseServlet
- Heberlein, A., Leggio, L., Stichtenoth, D., & Thomas, H. (2012). The treatment of alcohol and opioid dependence in pregnant women. *Current Opinion in Psychiatry*, 25(6), 559.
- Hemmings, H. C., & Egan, T. D. (2012). Pharmacology and physiology for anesthesia: foundations and clinical application. Elsevier Health Sciences.
- Hoffman, M. D., & Gelman, A. (2014). The No-U-turn sampler: adaptively setting path lengths in Hamiltonian Monte Carlo. *Journal of Machine Learning Research*, *15*(1), 1593–1623.
- Hser, Y.-I., Hoffman, V., Grella, C. E., & Anglin, M. D. (2001). A 33-Year Follow-up of Narcotics Addicts. Archives of General Psychiatry, 58(5), 503–508. https://doi.org/10.1001/archpsyc.58.5.503
- Hughes, K., Bellis, M. A., Hardcastle, K. A., Sethi, D., Butchart, A., Mikton, C., ... Dunne, M. P. (2017). The effect of multiple adverse childhood experiences on

health: a systematic review and meta-analysis. *The Lancet Public Health*, 2(8), e356–e366.

- IQVIA. (2018). Medicine Use and Spending in the U.S.: A Review of 2017 and Outlook to 2022. Retrieved from https://www.iqvia.com/institute/reports/medicine-useand-spending-in-the-us-review-of-2017-outlook-to-2022
- Ishwaran, H., & Rao, J. S. (2005). Spike and slab variable selection: frequentist and Bayesian strategies. *The Annals of Statistics*, *33*(2), 730–773.
- Johnson, E. M., Lanier, W. A., Merrill, R. M., Crook, J., Porucznik, C. A., Rolfs, R. T., & Sauer, B. (2013). Unintentional prescription opioid-related overdose deaths: description of decedents by next of kin or best contact, Utah, 2008–2009. *Journal* of General Internal Medicine, 28(4), 522–529.
- Jones, C. M. (2013). Trends in the distribution of selected opioids by state, US, 1999– 2011. *National Meeting Safe State Alliance*.
- Jones, C. M., Campopiano, M., Baldwin, G., & McCance-Katz, E. (2015, July 9). National and State Treatment Need and Capacity for Opioid Agonist Medication-Assisted Treatment [research-article]. https://doi.org/10.2105/AJPH.2015.302664
- Kane, J. M., Colvin, J. D., Bartlett, A. H., & Hall, M. (2018). Opioid-Related Critical Care Resource Use in US Children's Hospitals. *Pediatrics*, e20173335. https://doi.org/10.1542/peds.2017-3335
- Katz, J. (2018, February 14). How a Police Chief, a Governor and a Sociologist WouldSpend \$100 Billion to Solve the Opioid Crisis The New York Times. RetrievedFebruary 19, 2018, from

https://www.nytimes.com/interactive/2018/02/14/upshot/opioid-crisis-

solutions.html

Kennedy-Hendricks, A., Gielen, A., McDonald, E., McGinty, E. E., Shields, W., & Barry, C. L. (2016). Medication sharing, storage, and disposal practices for opioid medications among US adults. *JAMA Internal Medicine*, *176*(7), 1027–1029.

Kennedy-Hendricks, A., Richey, M., McGinty, E. E., Stuart, E. A., Barry, C. L., & Webster, D. W. (2016). Opioid Overdose Deaths and Florida's Crackdown on Pill Mills. *American Journal of Public Health*, *106*(2), 291–297. https://doi.org/10.2105/AJPH.2015.302953

- Kertesz, S., Manhapra, A., Olivia, E., & Sandbrink, F. (2018, April). VA Data about Prescription Opioids and Overdose and Suicide: Clinical Implications. Presented at the National Prescription Drug Abuse and Heroin Summit. Retrieved from https://www.scribd.com/document/375496421/VA-April-4th-Data-Opioids-Suicides
- Kiff, C. J., Lengua, L. J., & Zalewski, M. (2011). Nature and Nurturing: Parenting in the Context of Child Temperament. *Clinical Child and Family Psychology Review*, 14(3), 251–301. https://doi.org/10.1007/s10567-011-0093-4
- Kim, H., Hartung, D., Jacob, L., McCarty, D., & McConnell, K. J. (2016). The Concentration of Opioid Prescriptions by Providers and Patients in the Oregon Medicaid Program. *Psychiatric Services (Washington, D.C.)*, 67(4), 397–404. https://doi.org/10.1176/appi.ps.201500116
- Ko, S. J., Ford, J. D., Kassam-Adams, N., Berkowitz, S. J., Wilson, C., Wong, M., ...
 Layne, C. M. (2008). Creating trauma-informed systems: Child welfare,
 education, first responders, health care, juvenile justice. *Professional Psychology:*

Research and Practice, *39*(4), 396–404. https://doi.org/10.1037/0735-7028.39.4.396

- Kolar, A. F., Brown, B. S., Haertzen, C. A., & Michaelson, B. S. (1994). Children of substance abusers: The life experiences of children of opiate addicts in methadone maintenance. *The American Journal of Drug and Alcohol Abuse*, 20(2), 159–171.
- Kolodny, A., Courtwright, D. T., Hwang, C. S., Kreiner, P., Eadie, J. L., Clark, T. W., & Alexander, G. C. (2015). The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. *Annual Review of Public Health*, 36, 559– 574.
- Krawczyk, N., Feder, K. A., Fingerhood, M. I., & Saloner, B. (2017). Racial and ethnic differences in opioid agonist treatment for opioid use disorder in a U.S. national sample. *Drug and Alcohol Dependence*, *178*, 512–518. https://doi.org/10.1016/j.drugalcdep.2017.06.009

Lamont, A. (2010). Effects of child abuse and neglect for children and adolescents.

- Levine, A. (2018, July 31). The Government's Solution To The Opioid Crisis Feels Like A War To Pain Patients. Retrieved from https://www.huffingtonpost.com/entry/government-crackdown-opioidprescriptions-pain-patients_us_5b51ec57e4b0fd5c73c4a42e
 Lumley, T. (2004). Analysis of complex survey samples. *Journal of Statistical Software*, 9(1), 1–19.
- Lyons-Ruth, K., Bureau, J.-F., Easterbrooks, M. A., Obsuth, I., & Hennighausen, K. (2013). Parsing the Construct of Maternal Insensitivity: Distinct Longitudinal

Pathways Associated with Early Maternal Withdrawal. *Attachment & Human Development*, *15*(0). https://doi.org/10.1080/14616734.2013.841051

- Marlowe, D., & Carey, S. (2012). Research update on family drug courts. Retrieved from http://www.nadcp.org/wpcontent/uploads/Reseach%20Update%20on%20Family%20Drug%20Courts%20-%20NADCP.pdf
- Maryland Behavioral Risk Factor Surveillance System. (2017). Adverse Childhood Experiences (ACEs) in Maryland: Data from the 2015 Maryland BRFSS.
 Statewide and county-level estimates for non-institutionalized Maryland adults age 18+. Retrieved from https://phpa.health.maryland.gov/ccdpc/Reports/Documents/MD-BRFSS/2015 MD BRFSS ACEs Data Tables.pdf
- Mayes, L. C., Feldman, R., Granger, R. H., Haynes, O. M., Bornstein, M. H., & Schottenfeld, R. (1997). The effects of polydrug use with and without cocaine on mother-infant interaction at 3 and 6 months. *Infant Behavior and Development*, 20(4), 489–502.
- McCall Jones, C., Baldwin, G. T., & Compton, W. M. (2017). Recent Increases in Cocaine-Related Overdose Deaths and the Role of Opioids. *American Journal of Public Health*, 107(3), 430–432. https://doi.org/10.2105/AJPH.2016.303627
- McCarthy, G., & Taylor, A. (1999). Avoidant/Ambivalent Attachment Style as a Mediator between Abusive Childhood Experiences and Adult Relationship Difficulties. *The Journal of Child Psychology and Psychiatry and Allied Disciplines*, 40(3), 465–477.

- McKeganey, N., Barnard, M., & McIntosh, J. (2002). Paying the price for their parents' addiction: meeting the needs of the children of drug-using parents. *Drugs: Education, Prevention and Policy*, 9(3), 233–246.
- McLellan, A. T., Lewis, D. C., O'Brien, C. P., & Kleber, H. D. (2000). Drug
 Dependence, a Chronic Medical Illness: Implications for Treatment, Insurance, and Outcomes Evaluation. *JAMA*, 284(13), 1689–1695.
 https://doi.org/10.1001/jama.284.13.1689
- Mikulincer, M., & Shaver, P. R. (2012). An attachment perspective on psychopathology. *World Psychiatry*, 11(1), 11–15.
- Miller, J. M., Stogner, J. M., Miller, B. L., & Blough, S. (2017). Exploring synthetic heroin: Accounts of acetyl fentanyl use from a sample of dually diagnosed drug offenders. *Drug and Alcohol Review*.
- Muhuri, P. K., Gfroerer, J. C., & Davies, M. C. (2013). Associations of nonmedical pain reliever use and initiation of heroin use in the United States. *CBHSQ Data Review*, 17.
- Murphy, S. L., Xu, J., Kochanek, K. D., & Arias, E. (n.d.). Mortality in the United States, 2017.
- Muskett, C. (2014). Trauma-informed care in inpatient mental health settings: A review of the literature. *International Journal of Mental Health Nursing*, *23*(1), 51–59. https://doi.org/10.1111/inm.12012
- Naqavi, M. R., Mohammadi, M., Salari, V., & Nakhaee, N. (2011). The relationship between childhood maltreatment and opiate dependency in adolescence and middle age. *Addiction & Health*, *3*(3–4), 92.

National Center for Injury Prevention Control. (2016). 10 Leading Causes of Injury Deaths by Age Group Highlighting Unintentional Injury Deaths, United States – 2014 (Vol. 2017). Retrieved from

https://www.cdc.gov/injury/wisqars/pdf/leading_causes_of_injury_deaths_highlig hting_unintentional_injury_2014-a.pdf

National Center for Trauma-Informed Care and Alternatives to Seclusion and Restraint.
 (2018). *Trauma-Informed Approach and Trauma-Specific Interventions*.
 Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/nctic/trauma-interventions

National Institute on Drug Abuse. (2017, September 15). Overdose Death Rates. Retrieved February 19, 2018, from https://www.drugabuse.gov/relatedtopics/trends-statistics/overdose-death-rates

- National Institute on Drug Abuse. (2018, August 9). Overdose Death Rates. Retrieved December 6, 2018, from https://www.drugabuse.gov/related-topics/trendsstatistics/overdose-death-rates
- National Institute on Drug Abuse. (2018, February 28). Florida Opioid Summary. Retrieved June 29, 2018, from https://www.drugabuse.gov/drugsabuse/opioids/opioid-summaries-by-state/florida-opioid-summary
- Neger, E. N., & Prinz, R. J. (2015). Interventions to address parenting and parental substance abuse: Conceptual and methodological considerations. *Clinical Psychology Review*, 39, 71–82.
- NPO Staff. (2018, July). LawAtlas Policy Surveillance Report, Query Report on Dataset: Query where At least one of these selections apply - Does this state have

legislation authorizing access by professionals to a PDMP system? Retrieved from lawaltas.org/preview?dataset=prescription-monitoring-program-laws-1408223332

- Nummenmaa, L., Manninen, S., Tuominen, L., Hirvonen, J., Kalliokoski, K. K., Nuutila, P., ... Sams, M. (2015). Adult attachment style is associated with cerebral μopioid receptor availability in humans. *Human Brain Mapping*, *36*(9), 3621–3628. https://doi.org/10.1002/hbm.22866
- Ompad, D. C., Ikeda, R. M., Shah, N., Fuller, C. M., Bailey, S., Morse, E., ... Vlahov, D. (2005). Childhood sexual abuse and age at initiation of injection drug use. *American Journal of Public Health*, 95(4), 703–709.
- Patrick, S. W., & Schiff, D. M. (2017). A Public Health Response to Opioid Use in Pregnancy. *Pediatrics*, e20164070.
- Patrick, S. W., Schumacher, R. E., Benneyworth, B. D., Krans, E. E., McAllister, J. M.,
 & Davis, M. M. (2012). Neonatal abstinence syndrome and associated health care expenditures: United States, 2000-2009. *Jama*, 307(18), 1934–1940.
- Peterson, L., & Brown, D. (1994). Integrating child injury and abuse-neglect research: common histories, etiologies, and solutions. *Psychological Bulletin*, *116*(2), 293.
- Price, R. K., Risk, N. K., & Spitznagel, E. L. (2001). Remission from drug abuse over a 25-year period: patterns of remission and treatment use. *American Journal of Public Health*, 91(7), 1107–1113.
- Proust-Lima, C., Philipps, V., & Liquet, B. (2015). Estimation of extended mixed models using latent classes and latent processes: the R package lcmm. *ArXiv Preprint ArXiv:1503.00890*.

- Quast, T., Storch, E. A., & Yampolskaya, S. (2018). Opioid Prescription Rates And Child Removals: Evidence From Florida. *Health Affairs*, 37(1), 134–139. https://doi.org/10.1377/hlthaff.2017.1023
- R Core Team. (2017). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from https://www.Rproject.org/
- R Core Team. (2017). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from https://www.Rproject.org/
- Racine, M. (2018). Chronic pain and suicide risk: A comprehensive review. Progress in Neuro-Psychopharmacology & Biological Psychiatry, 87(Pt B), 269–280. https://doi.org/10.1016/j.pnpbp.2017.08.020

Radel, L., Baldwin, M., Crouse, G., Ghertner, R., & Waters, A. (2018a). Medication-Assisted Treatment for Opioid Use Disorder in the Child Welfare Context: Challenges and Opportunities. Retrieved from ASPE website: https://aspe.hhs.gov/pdf-report/medication-assisted-treatment-opioid-usedisorder-child-welfare-context-challenges-and-opportunities

Radel, L., Baldwin, M., Crouse, G., Ghertner, R., & Waters, A. (2018). Substance use, the opioid epidemic, and the child welfare system: Key Findings from a Mixed Methods Study. *ASPE*. Retrieved from https://aspe.hhs.gov/system/files/pdf/258836/SubstanceUseChildWelfareOvervie w.pdf

- Reavis, J. A., Looman, J., Franco, K. A., & Rojas, B. (2013). Adverse Childhood
 Experiences and Adult Criminality: How Long Must We Live before We Possess
 Our Own Lives? *The Permanente Journal*, *17*(2), 44–48.
 https://doi.org/10.7812/TPP/12-072
- Rees, D. I., Sabia, J. J., Argys, L. M., Latshaw, J., & Dave, D. (2017). With a Little Help from My Friends: The Effects of Naloxone Access and Good Samaritan Laws on Opioid-Related Deaths (Working Paper No. 23171). National Bureau of Economic Research. https://doi.org/10.3386/w23171
- Renk, K., Boris, N. W., Kolomeyer, E., Lowell, A., Puff, J., Cunningham, A., ...
 McSwiggan, M. (2015). The state of evidence-based parenting interventions for parents who are substance-involved. *Pediatric Research*, 79(1–2), 177–183.
- Rick, A. D., Vanheule, S., & Verhaeghe, P. (2009). Alcohol Addiction and the
 Attachment System: An Empirical Study of Attachment Style, Alexithymia, and
 Psychiatric Disorders in Alcoholic Inpatients. *Substance Use & Misuse*, 44(1),
 99–114. https://doi.org/10.1080/10826080802525744
- Robins, L. N., & Slobodyan, S. (2003). Post-Vietnam heroin use and injection by returning US veterans: clues to preventing injection today. *Addiction*, 98(8), 1053–1060. https://doi.org/10.1046/j.1360-0443.2003.00436.x
- Roddy, J., & Greenwald, M. (2009). An economic analysis of income and expenditures by heroin-using research volunteers. *Substance Use & Misuse*, 44(11), 1503–1518.
- Rubin, D. B. (1976). Inference and missing data. *Biometrika*, 63(3), 581–592.

- Rutkow, L., Chang, H.-Y., Daubresse, M., Webster, D. W., Stuart, E. A., & Alexander,
 G. C. (2015). Effect of Florida's Prescription Drug Monitoring Program and Pill
 Mill Laws on Opioid Prescribing and Use. *JAMA Internal Medicine*, *175*(10),
 1642. https://doi.org/10.1001/jamainternmed.2015.3931
- Ryan, S. A., Gonzalez, P. K., Patrick, S. W., Quigley, J., Siqueira, L., & Walker, L. R. (2016). Medication-assisted treatment of adolescents with opioid use disorders. *Pediatrics*, 138(3), e20161893.
- Saitz, R., Larson, M. J., LaBelle, C., Richardson, J., & Samet, J. H. (2008). The Case for Chronic Disease Management for Addiction. *Journal of Addiction Medicine*, 2(2), 55–65. https://doi.org/10.1097/ADM.0b013e318166af74

SAMHSA. (n.d.). SAMHDA. Retrieved from https://www.datafiles.samhsa.gov/

Scott, S. L. (2017, July 11). Fitting Bayesian structural time series with the bsts R package. Retrieved from

http://www.unofficialgoogledatascience.com/2017/07/fitting-bayesian-structuraltime-series.html

- Scott, S. L., & Varian, H. R. (2014). Predicting the present with bayesian structural time series. *International Journal of Mathematical Modelling and Numerical Optimisation*, 5(1–2), 4–23.
- Seth, P. (2018). Overdose Deaths Involving Opioids, Cocaine, and Psychostimulants United States, 2015–2016. MMWR. Morbidity and Mortality Weekly Report, 67. https://doi.org/10.15585/mmwr.mm6712a1
- Stan Development Team. (2018). *Stan Modeling Language Users Guide and Reference Manual*. Retrieved from http://mc-stan.org/users/documentation/

Stedt, E. V., & DeCerchio, K. (2016, August). Regional Partnership Grants Collaborative Approaches: Lessons Learned from the RPG Program. Presented at the Child Welfare League of America National Conference, Orange County, California, USA. Retrieved from https://www.cwla.org/wpcontent/uploads/2016/09/D3_Workshop_RPG_Final.pdf

- Thorberg, F. A., & Lyvers, M. (2006). Attachment, fear of intimacy and differentiation of self among clients in substance disorder treatment facilities. *Addictive Behaviors*, 31(4), 732–737. https://doi.org/10.1016/j.addbeh.2005.05.050
- Tracy, K., & Wallace, S. P. (2016). Benefits of peer support groups in the treatment of addiction. Substance Abuse and Rehabilitation, 7, 143–154. https://doi.org/10.2147/SAR.S81535
- Traube, D. E. (2012). The Missing Link to Child Safety, Permanency, and Well-Being:
 Addressing Substance Misuse in Child Welfare. *Social Work Research*, *36*(2),
 83–87. https://doi.org/10.1093/swr/svs043
- Ulmer, J. T., & Steffensmeier, D. (2014). The age and crime relationship: Social variation, social explanations. In *The nurture versus biosocial debate in criminology: On the origins of criminal behavior and criminality*. SAGE Publications Inc.
- van Buuren, S., & Groothuis-Oudshoorn, K. (2011). mice: Multivariate Imputation by Chained Equations in R. *Journal of Statistical Software*, *45*(3), 1–67.
- van de Schoot, R., Kaplan, D., Denissen, J., Asendorpf, J. B., Neyer, F. J., & van Aken, M. A. G. (2014). A gentle introduction to bayesian analysis: applications to

developmental research. *Child Development*, 85(3), 842–860. https://doi.org/10.1111/cdev.12169

- Vanderploeg, J. J., Connell, C. M., Caron, C., Saunders, L., Katz, K. H., & Tebes, J. K. (2007). The impact of parental alcohol or drug removals on foster care placement experiences: A matched comparison group study. *Child Maltreatment*, 12(2), 125–136. https://doi.org/10.1177/1077559507299292
- Vehtari, A., Gelman, A., & Gabry, J. (2017). Practical Bayesian model evaluation using leave-one-out cross-validation and WAIC. *Statistics and Computing*, 27(5), 1413– 1432.
- Vlahov, D., Anthony, J. C., Munoz, A., Margolick, J., Nelson, K. E., Celentano, D. D., ... Polk, B. F. (1991). The ALIVE study, a longitudinal study of HIV-1 infection in intravenous drug users: description of methods and characteristics of participants. *NIDA Research Monograph*, (109), 75–100.
- Volkow, N. D., Frieden, T. R., Hyde, P. S., & Cha, S. S. (2014). Medication-assisted therapies—tackling the opioid-overdose epidemic. *New England Journal of Medicine*, 370(22), 2063–2066.
- Weiss, R. D., Potter, J. S., Fiellin, D. A., Byrne, M., Connery, H. S., Dickinson, W., ... Ling, W. (2011). Adjunctive counseling during brief and extended buprenorphinenaloxone treatment for prescription opioid dependence: a 2-phase randomized controlled trial. *Archives of General Psychiatry*, 68(12), 1238–1246. https://doi.org/10.1001/archgenpsychiatry.2011.121
- Wellisch, D. K., & Steinberg, M. R. (1980). Parenting attitudes of addict mothers. *International Journal of the Addictions*, 15(6), 809–819.

- Wen, H., Druss, B. G., & Cummings, J. R. (2015). Effect of Medicaid Expansions on Health Insurance Coverage and Access to Care among Low-Income Adults with Behavioral Health Conditions. *Health Services Research*, 50(6), 1787–1809.
- Wolf, J. P., Ponicki, W. R., Kepple, N. J., & Gaidus, A. (2016). Are community level prescription opioid overdoses associated with child harm? A spatial analysis of California zip codes, 2001–2011. *Drug and Alcohol Dependence*, 166, 202–208.
- Wong, S., Ordean, A., Kahan, M., Gagnon, R., Hudon, L., Basso, M., ... Delisle, M.-F. (2011). Substance use in pregnancy. *Journal of Obstetrics and Gynaecology Canada*, 33(4), 367–384.
- Wulczyn, F., Ernst, M., & Fisher, P. (2011). Who are the Infants in Out-of-home Care?: An Epidemiological and Developmental Snapshot. Chapin Hall.
- Young, K. A., Liu, Y., Gobrogge, K. L., Wang, H., & Wang, Z. (2014). Oxytocin reverses amphetamine-induced deficits in social bonding: evidence for an interaction with nucleus accumbens dopamine. *Journal of Neuroscience*, 34(25), 8499–8506.
- Younger, J. W., Chu, L. F., D'Arcy, N. T., Trott, K. E., Jastrzab, L. E., & Mackey, S. C. (2011). Prescription opioid analgesics rapidly change the human brain. *PAIN®*, *152*(8), 1803–1810.

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- 2017 Center on Behavioral Health Quality and Statistics Substance Abuse and Mental Health Services Administration U.S. Department of Health and Human Services Summer Intern
- **2014-2015 Connecticut Voices for Children** Policy Analyst
- **2012-2014 Connecticut Voices for Children** Policy Fellow

Research Funding and Scholarships

2017-2019 Children	Collateral Consequences of the United States Opioid Epidemic for
	NIH NIDA F31 DA044699 (\$88,000) Role: Principal Investigator
2017 2010	

- **2017-2019** Childhood Adversity in the United States Opioid Epidemic Doris Duke Foundation Fellowship for the Promotion of Child Wellbeing (\$60,000) Role: Fellow (Cohort 7)
- 2015-2017 Mental Health Scholar Award Department of Mental Health Johns Hopkins Bloomberg School of Public Health Tuition and Health Insurance Scholarship (\$100,000)

Awards and Honors

2017 Health	Paul V. Lemkau Scholarship Fund Department of Mental Health, Johns Hopkins Bloomberg School of Public
	Award for Service to Department (\$10,000)
2014	Connecticut Health Foundation Health Leadership Fellowship Competitive training program for Connecticut leaders in health equity Awarded for work on Medicaid policy

Teaching Experience

2018	Psychiatric Epidemiology Department of Mental Health Johns Hopkins Bloomberg School of Public Health Teaching Assistant (Instructors: William Eaton and Heather Volk)
2017	Public Mental Health Department of Mental Health Johns Hopkins Bloomberg School of Public Health Teaching Assistant (Instructor: M. Daniele Fallin)
2017-2018	Principles of Epidemiology Department of Epidemiology Johns Hopkins Bloomberg School of Public Health Tutor (Department of Mental Health)
2016-2018	Biostatistical Methods Department of Biostatistics Johns Hopkins Bloomberg School of Public Health Tutor (all departments)
2016-2018	Statistical Methods in Public Health Department of Biostatistics Johns Hopkins Bloomberg School of Public Health Tutor (all departments)
Service and V	Volunteer Experience
2018-Present	American Professional Society on the Abuse of Children APSAC Advisor Referee: Contested Issue on Opioid Use in Pregnancy
2017-Present	Center for the Study of Social Policy Systems Change Team Co-Author: White Paper on Opioid Crisis and Child Welfare
2016-2018	Baltimore City Department of Social Services Analyst (volunteer)
2015	Connecticut Health Foundation Health Leadership Fellowship

- Riehm, K.E., Young, A.S., Feder, K.A., Krawczyk, N., Tormohlen, K., Pacek, .R., Mojtabai, R., & Crum, R.M. (in press). Mental Health Problems and Initiation of E-Cigarette and Combustible Cigarette Use. *Pediatrics*.
- Boggis, J. S., & Feder, K.A. (2019). Trends in and Correlates of Tranquilizer Misuse Among Adults Who Misuse Opioids in the United States, 2002–2014. *Drug and Alcohol Dependence*.
- Novak, P., Feder, K. A., Ali, M. M., & Chen, J. (2019). Behavioral health treatment utilization among individuals with co-occurring opioid use disorder and mental illness: Evidence from a national survey. *Journal of Substance Abuse Treatment*, 98, 47–52. https://doi.org/10.1016/j.jsat.2018.12.006
- Feder, K. A., Letourneau, E. J., & Brook, J. (2018). Children in the Opioid Epidemic: Addressing the Next Generation's Public Health Crisis. *Pediatrics*, e20181656. https://doi.org/10.1542/peds.2018-1656
- Feder, K. A., Krawczyk, N., Mojtabai, R., Crum, R. M., Kirk, G., & Mehta, S. H. (2019). Health insurance coverage is associated with access to substance use treatment among individuals with injection drug use: Evidence from a 12-year prospective study. Journal of Substance Abuse Treatment, 96, 75–81.
- Feder, K. A., Mojtabai, R., Musci, R. J., & Letourneau, E. J. (2018). U.S. adults with opioid use disorder living with children: Treatment use and barriers to care. *Journal of Substance Abuse Treatment*, 93, 31–37.
- Feder, K.A., Heatherington, L., Mojtabai, R., & Eaton, W.W. (2018) Perceived Marital Support and Incident Mental Illness: Evidence from a Two-Wave National Survey of the United States. *Journal of Marriage and Family Therapy*,
- Holingue, C., Owusu, J.T., Feder, K.A., & Spira, A.P. (2018) Sleep duration and Creactive protein: Associations among pregnant and non-pregnant women, *Journal* of Reproductive Immunology, 128, 9-15.
- Mojtabai, R., Feder, K.A., Kealhofer, M., Krawczyk, N., Storr, C., Tormohlen, K.N., Young, A.S., Olfson, M. & Crum, R.M. (2018). State variations in Medicaid enrollment and utilization of substance use services: Results from a National Longitudinal Study. *Journal of Substance Abuse Treatment*, 89, 75-86.
- Feder, K.A., McCart, M.R., Kahn, G., Mauro, P.M., Sheidow, A.J., & Letourneau, E.J. (2018). Association of Mental Health Symptoms and Peer Behaviors with Risk for Substance Use and Condomless Sex among Youth in Juvenile Drug Court. *Journal of Child and Adolescent Substance Abuse*, 27(3), 133-145.

- Krawczyk, N., Picher, C.E., Feder, K.A., & Saloner, B. (2017). Only One in Twenty Justice-Referred Adults in Specialty Treatment for Opioid Use Receive Methadone or Buprenorphine. *Health Affairs*, 36(12), 2046-2053. Selected as One of Best 10 Papers of Year by Health Affairs' Editor.
- Feder, K.A., Mojtabai, R., Krawczyk, N., Young, A.S., Kealhofer, M., Tormohlen, K.N., & Crum, R.M (2017). Trends in Insurance Coverage and Treatment Among Persons with Opioid Use Disorders Following the Affordable Care Act. *Drug and Alcohol Dependence*, 179, 271-274.
- Krawczyk, N., Feder, K.A., Fingerhood, M.I., & Saloner, B. (2017). Racial and Ethnic Differences in Opioid Agonist Treatment for Opioid Use Disorder in a U.S. National Sample. *Drug and Alcohol Dependence*, 178, 512-518.
- Saloner, B., Feder, K.A., & Krawczyk, N. (2017). Closing the Medication-Assisted Treatment Gap for Youth with Opioid Use Disorder. JAMA Pediatrics, 171(8):729-731
- Feder, K.A., Krawczyk, N., & Saloner B. (2017). Medication assisted treatment for adolescents in specialty treatment for opioid use disorder. *Journal of Adolescent Health*, 60(6), 747-750.
- Krawczyk, N., Feder, K.A., Saloner, B., Crum, R.M., Kealhofer, M., & Mojtabai, R. (2017). The association of psychiatric comorbidity with treatment completion among clients admitted to substance use treatment programs in a U.S. national sample. *Drug and Alcohol Dependence*, 175, 157-163.
- Letourneau, E.J., Schaeffer, C.M., Bradshaw, C.P., & Feder, K.A. (2017) Preventing the Onset of Child Sexual Abuse by Targeting Young Adolescents with Universal Prevention Programming. *Child Maltreatment*, 22(2), 100-111.

Book Chapters

Shields, R.T & Feder, K.A. (2017). The public health approach to preventing sexual violence. In Jeglic, E.L., Calkins, C. (Eds.), *Sexual Violence: Evidence Based Policy and Prevention*.

Popular Media

Feder, K.A. & Krawczyk, N. (2017). Four facts every journalist should know when covering the opioid epidemic. *Columbia Journalism Review*. August 15, 2017. Available at https://www.cjr.org/local_news/opioid-journalist-advice.php.

- Feder, K.A. (2015) "State Must Direct Aid to Neediest Schools." *The Hartford Courant*. March 30th, 2015. Available at <u>http://www.courant.com/opinion/op-ed/hc-op-feder-connecticut-school-aid-for-poor-0331-20150330-story.html</u>.
- Feder, K.A. (2014) "CHEER an important step... but Connecticut can do better." The Connecticut Mirror. July 3, 2014. Available at <u>http://ctmirror.org/2014/07/03/cheer-an-important-step-but-connecticut-can-dobetter/</u>.

Presentations & Posters

- Feder, K.A. (2018). *Children and Families in the Opioid Epidemic*. Lecture presented at the American Professional Society on the Abuse of Children Annual Colloquium, San Diego, CA.
- Feder, K.A., Krawczyk, N., Mojtabai, R., Crum, R.M., Kirk, G.D., & Mehta, Shruti H. (2018). Acquiring Insurance Coverage is Associated with Accessing Substance Use Treatment among People who Inject Drugs. Poster presented at the College on Problems for Drug Dependence Annual Meeting, San Diego, CA.
- Feder K.A. (2017). Descriptive Epidemiology of Families Affected by the United States' Opioid Epidemic. Poster presented at the Moore Center for the Prevention of Child Sexual Abuse Annual Symposium, Johns Hopkins University, Baltimore, MD.
- Feder K.A. & Krawczyk N. (2017). Unseen Populations and Unmet Need in the United States Opioid Epidemic. Lecture presented at the Johns Hopkins Bloomberg School of Public Health, Department of Mental Health Weekly Seminar, Baltimore, MD.
- Feder K.A. (2016). DSM-IV diagnoses associated with perpetrating child maltreatment in a nationally representative sample. Poster presented at the Moore Center for the Prevention of Child Sexual Abuse Annual Symposium, Johns Hopkins University, Baltimore, MD.
- Krawczyk, N., Feder, K.A. (2016). Racial and Ethnic Disparities in Opioid Agonist Treatment for Opioid Use Disorder in a U.S. National Sample. Poster presented at the annual meeting of the College on Problems of Drug Dependence, Montreal, Canada.
- Lloyd, S., Pollack, L., Feder, K.A., Daniels, M., Greenblatt, A., Leaf, P. (2016) Neighborhood context and the rate of child welfare contact: An evaluation and synthesis of population based research. Poster presented at the annual meeting of the American Public Health Association, Denver, CO.

- Lee, M.A., Feder, K.A., & Langer, S. (2015). "Births to Mothers with HUSKY Program Coverage (Medicaid and CHIP): 2011." *Connecticut Voices for Children*. Available at <u>http://www.ctvoices.org/publications/births-mothers-husky-program-</u> coverage-medicaid-and-chip-2011.
- Lee, M.A. & Feder, K.A. (2015). "Children's Healthcare in the HUSKY Program: Impact of Converting Managed Care to an Administered Fee-for-Service Medicaid Program." *Connecticut Voices for Children*. Available at <u>http://www.ctvoices.org/publications/childrens-health-care-husky-program-impact-converting-risk-based-managed-care-administe</u>.
- Lee, M.A. & Feder, K.A. (2015). "Dental Services for Children and Parents in the HUSKY Program in 2013: Utilization is Improved Over 2008 but Unchanged from 2012." Connecticut Voices for Children. Available at <u>http://www.ctvoices.org/publications/dental-services-children-and-parents-huskyprogram-2013-utilization-improved-over-2008-.</u>
- Lee, M.A., Feder, K.A., & Langer, S. (2015). "Coverage Continuity in the HUSKY Program Increases Children's Preventive Medical and Dental Care Utilization." *Connecticut Voices for Children*. Available at <u>http://www.ctvoices.org/publications/coverage-continuity-husky-program-increases-childrens-preventive-medical-and-dental-car.</u>
- Feder, K.A., Iverson, S., & Oppenheimer, C. (2015). "Unequal Schools: Connecticut's Racial, Socioeconomic, and Geographic Disparities in Kindergarten Class Size and Teaching Experience." *Connecticut Voices for Children*. Available at <u>http://www.ctvoices.org/publications/unequal-schools-connecticuts-racialsocioeconomic-and-geographic-disparities-kindergart</u>.
- Joseph, E. & Feder, K.A. (2014). "Because Relationships Matter: Improving Opportunities and Outcomes for Youth in Foster Care." *Connecticut Voices for Children*. Available at <u>http://www.ctvoices.org/publications/because-</u> relationships-matter-improving-opportunities-and-outcomes-youth-foster-care.
- Feder, K.A. (2014). "Connecticut's Invisible Opportunity Gap: The Academic Experience of Children and Youth in Foster Care." Connecticut Voices for Children. Available at <u>http://www.ctvoices.org/publications/connecticuts-</u> invisible-opportunity-gap-academic-challenges-facing-children-and-youth-fo.

- Lee, M.A., Feder, K.A., & Learned, A. (2014). "Dental Services for Children and Parents in the HUSKY Program in 2012: Utilization is Improved Over 2008 but Unchanged from 2011." Connecticut Voices for Children. Available at <u>http://www.ctvoices.org/publications/dental-services-children-and-parents-husky-program-2012-utilization-improved-over-2008-</u>.
- Cotto Jr., R. & Feder, K.A. (2014). "Choice Watch: Diversity and Access in Connecticut's School Choice Programs." *Connecticut Voices for Children*. Available at <u>http://www.ctvoices.org/publications/choice-watch-diversity-and-access-connecticuts-school-choice-programs</u>.
- Feder, K.A. & Kramer, T. (2013). "Raise the Grade: Improving Educational Opportunities for Children in State Care." *Connecticut Voices Children*. Available at <u>http://www.ctvoices.org/publications/raise-grade-improving-educational-opportunities-children-state-care</u>.
- Feder, K.A. & Langer, S. (2013). "Health Reform Provides New Health Coverage for Youth Formerly in Foster Care." *Connecticut Voices for Children*. Available at <u>http://www.ctvoices.org/publications/health-reform-provides-new-health-coverage-youth-formerly-foster-care</u>.
- Lee, M.A., Feder, K.A., & Learned, A. (2013). "Dental Services for Children and Parents in the HUSKY Program: Utilization Continues to Increase Since Program Improvements in 2008." Connecticut Voices for Children. Available at <u>http://www.ctvoices.org/publications/dental-services-children-and-parents-husky-program-utilization-continues-increase-progr.</u>
- Feder, K.A. (2013). "The Impact of the Governor's Proposed Municipal Aid Budget on Education, Towns, and Children." *Connecticut Voices for Children*. Available at <u>http://www.ctvoices.org/publications/impact-governors-proposed-municipal-aidbudget-education-towns-and-children</u>.
- Feder, K.A. & Rodriguez O. (2013). "The State of Working Connecticut 2012: Employment, Jobs, and Wages in the Wake of the Great Recession." Connecticut Voices for Children. Available at <u>http://www.ctvoices.org/publications/state-</u> working-connecticut-2012-employment-jobs-and-wages-wake-great-recession.

Legislative Testimony

Feder, K.A. & Leventhal-Weiner, R. "Testimony Regarding S.B. 816: An Act Concerning a Minimum Level of Funding Under the Education Cost Sharing Formula." Hearing before the Committee on Appropriations, Connecticut General Assembly. April 2, 2015. Available at <u>http://www.ctvoices.org/sites/default/files/040215_approps_sb816_ecsmin50pct.p_df</u>.

- Feder, K.A. & Leventhal-Weiner, R. "Testimony Regarding S.B. 1096: An Act Concerning Charter Schools." *Connecticut Voices for Children*. Hearing before the Committee on Education, Connecticut General Assembly. March 19, 2015. Available at <u>http://www.ctvoices.org/sites/default/files/031915_edu_sb1096_charterschools.pd</u> <u>f</u>
- Defiesta, N., Shemitz, E., and Feder, K.A. "Testimony Regarding H.B 5411: An Act Concerning Disproportionate Liability Under the Personal Income Tax. Testimony Opposing New Tax Expenditures in H.B. 5561, H.B. 5655, H.B. 6535, H.B. 6536." Hearing before the Finance, Revenue, and Bonding Committee, Connecticut General Assembly. March 18, 2015. Available at <u>http://www.ctvoices.org/sites/default/files/031815_finrevbond_hb5411_hb5561_h</u> <u>b5655_hb6535_hb6536_taxes.pdf</u>.
- Feder, K.A., Defiesta, N., and Shemitz, E. "Testimony Supporting S.B. 1044: An Act Concerning Recoupment of State Costs Attributable to Low-Wage Workers." *Connecticut Voices for Children*. Hearing before the Committee on Human Services, Connecticut General Assembly. March 12, 2015. Available at <u>http://www.ctvoices.org/sites/default/files/031215_humansvcs_sb1044_recoupcos</u> <u>tlowwageearners.pdf</u>
- Feder, K.A. & Leventhal-Weiner, R. "Testimony Supporting S.B. 1056: An Act Concerning the Excess Cost Threshold and the Collection of Data Relating to Per-Pupil Costs of Special Education." *Connecticut Voices for Children*. Hearing before the Committee on Education, Connecticut General Assembly. March 11, 2015. Available at <u>http://www.ctvoices.org/advocacy/legislative-testimony</u>.
- Joseph, E. & Feder, K.A. "Testimony Regarding H.B. 6824: An Act Concerning the State Budget for the Biennium Ending June Thirtieth 2017, and Making Appropriations Therefore and Other Provisions Related to Revenue." Connecticut Voices for Children. Hearing before the Committee on Appropriations, Connecticut General Assembly. March 5, 2015. Available at http://www.ctvoices.org/advocacy/legislative-testimony?page=1.
- Feder, K.A. & Leventhal-Weiner, R. "Testimony Regarding the Governor's Proposed Budget for K-12 Education." *Connecticut Voices for Children*. Hearing before the Committee on Appropriations, Connecticut General Assembly. March 3, 2015. Available at http://www.ctvoices.org/sites/default/files/030515 approps govk12budget.pdf.

- Leventhal-Weiner, R. & Feder, K.A. "Testimony Supporting H.B. 6835: An Act Concerning English Language Learners." *Connecticut Voices for Children*. Hearing before the Committee on Education, Connecticut General Assembly. February 25, 2015. Available at <u>http://www.ctvoices.org/sites/default/files/022515_edu_hb6835_englanglearners.</u> <u>pdf</u>.
- Feder, K.A. "Testimony Supporting S.B. 843: An Act Concerning Trauma Informed Practice Training for Teachers, Administrators, and Pupil Personnel." *Connecticut Voices for Children*. Hearing before the Committee on Children, Connecticut General Assembly. February 24, 2015. Available at <u>http://www.ctvoices.org/sites/default/files/022515_children_sb843_traumainform</u> <u>edtraining.pdf</u>.
- Feder, K.A. "Testimony Regarding H.B. 6763: An Act Concerning Social Innovation." Connecticut Voices for Children. Hearing before the Committee on Human Services, Connecticut General Assembly, February 19, 2015. Available at <u>http://www.ctvoices.org/sites/default/files/021915_humansvc_hb5743_socialinno_vation.pdf</u>.
- Feder, K.A. "Testimony Supporting S.B. 842: An Act Concerning Foster Children and the Designation of Surrogate Parents." *Connecticut Voices for Children*. Hearing before the Committee on Children, Connecticut General Assembly, February 17, 2015. Available at <u>http://www.ctvoices.org/sites/default/files/021715_children_sb842_fosterchildsur</u> <u>rogateparent.pdf</u>.
- Feder, K.A. & Langer, S. "Testimony Regarding S.B. 851: An Act Concerning the Eligibility of Children Enrolled in the HUSKY Program." Hearing before the Committee on Human Services, Connecticut General Assembly, February 10, 2015. Available at <u>http://www.ctvoices.org/sites/default/files/021015_humansvc_sb851_huskyeligibi lity.pdf</u>.
- Feder, K.A. "Testimony Regarding S.B. 311: An Act Concerning Notification of Boards of Education on the Placement of Certain Children in the School District." Hearing before the Committee on Children, Connecticut General Assembly, February 5, 2015. Available at <u>http://www.ctvoices.org/sites/default/files/020515_children_sb311_boenotificatio_nplacement.pdf</u>.
- Feder, K.A. "Testimony Regarding H.B. 6393: An Act Concerning State Support to Grandparents who are Raising Children." Hearing before the Committee on Aging, Connecticut General Assembly, February 5, 2015. Available at <u>http://www.ctvoices.org/sites/default/files/020515_aging_hb6393_supporttogrand</u> <u>parents.pdf</u>.

- Joseph, E., Feder, K.A., & Oppenheimer, C. "Testimony Regarding S.B. 476: An Act Concerning the Academic Achievement Gap." Hearing before the Committee on Education, Connecticut General Assembly, March 17, 2014. Available at <u>http://www.ctvoices.org/sites/default/files/031414_edu_sb476_achievementgap.p</u> <u>df</u>
- Joseph, E., Feder, K.A., & Oppenheimer, C. "Testimony in Support of S.B. 424: An Act Concerning Access to Preschool Programs for Children in the Care and Custody of the Department of Children and Families." Hearing before the Committee on Education, Connecticut General Assembly, March 12, 2014. Available at <u>http://www.ctvoices.org/sites/default/files/031214_edu_sb424_hb5522_preschool</u> <u>dcf_schoolreadiness.pdf</u>
- Feder, K.A. & Joseph, E. "Testimony in Support of S.B. 366: An Act Concerning Erasure of Records in Delinquency and Family with Service Need Matters." Hearing before the Committee on the Judiciary, Connecticut General Assembly, March 10, 2014. Available at <u>http://www.ctvoices.org/sites/default/files/031014_judic_sb366_erasureofdelinqre_cords.pdf</u>.
- Feder, K.A. "Testimony Regarding H.B. 5304: An Act Preventing Homelessness of Youth Under the Care of the Commissioner of Children and Families." Hearing before the Committee on Children, Connecticut General Assembly, March 6, 2014. Available at http://www.ctvoices.org/sites/default/files/030314_children_hb5304_preventhom elessnessdcfyouth.pdf.
- Feder, K.A. "Testimony Regarding H.B. 5374: An Act Implementing the Recommendations of the Program Review and Investigations Committee on the Department of Children and Families as they Relate to Preparation of Youths Aging Out of State Care." Hearing before the Program Review and Investigations Committee, Connecticut General Assembly, March 4, 2014. Available at <u>http://www.ctvoices.org/sites/default/files/030414_pric_hb5374_youthageoutfoste</u> rcare.pdf.
- Feder, K.A. "Testimony Supporting S.B. 203: An Act Concerning a Statewide Sexual Abuse and Assault Awareness Program." Feder, K.A. & Langer, Sharon. Hearing before the Committee on Children, Connecticut General Assembly, February 27, 2014. Available at <u>http://www.ctvoices.org/sites/default/files/022714_children_sb203_sexualabusea</u> warenessprogram.pdf.
- Feder, K.A., Santacroce, M., & Langer, S. Testimony Opposing Reduced Appropriations to the Department of Children and Families. Hearing before the Committee on Appropriations, Connecticut General Assembly, February 14, 2014. Available at

http://www.ctvoices.org/sites/default/files/021414_approps_reducedappropsdcf.p df.

- Feder, K.A. "Testimony Regarding DCF Services to Prepare Youth Aging Out of State Care," Hearing before the Program Review and Investigations Committee, Connecticut General Assembly, October 3, 2013. Available at http://www.ctvoices.org/sites/default/files/100313 pric dcfagingoutstatecare.pdf.
- Feder, K.A. & Geballe, S. "Testimony Regarding Governor's H.B. 6367: An Act Implementing the Governor's Budget Recommendations for Human Services Programs." Hearing before the Committee on Human Services, Connecticut General Assembly, February 26, 2013. Available at <u>http://www.ctvoices.org/sites/default/files/022613_humanservices_hb6367_fundingfosteringconnections.pdf</u>.
- Feder, K.A. & Geballe, S. "Testimony Regarding The Governor's Proposed Budget for the Department of Children and Families." Hearing before the Committee on Appropriations, Connecticut General Assembly, February 22, 2013. Available at <u>http://www.ctvoices.org/sites/default/files/022613_humanservices_hb6367_fundi_ngfosteringconnections.pdf</u>.
- Feder, K.A. & Esty, S. "Testimony Supporting Raised H.B. 6399: An Act Concerning Children in the Juvenile Justice System." Hearing before the Committee on Children, Connecticut General Assembly, February 21, 2013. Available at <u>http://www.ctvoices.org/sites/default/files/022113_childrens_hb6399_shackling_e</u> rasure timeserved questioning.pdf.
- Feder, K.A. "Testimony Supporting S.B. 273: An Act Concerning Foster Children and Internship Opportunities; Testimony Supporting S.B. 652: An Act Concerning Referrals from the Department of Children and Families to the Birth-to-Three Program; Testimony Opposing S.B. 653: An Act Concerning the Department of Children and Families and Out-of-State Placement for Children Under the Purview of Such Agency." Hearing before the Committee on Children, Connecticut General Assembly, February 14, 2013. Available at <u>http://www.ctvoices.org/sites/default/files/021413_childrens_sb273_sb652_sb653</u> <u>birthtothreereferrals_outofstateplacements_internships.pdf.</u>
- Feder, K.A. "Testimony Supporting H.B. 5764: An Act Increasing Temporary Family Assistance for Grandparents and Other Nonparent Relative Caretakers." Hearing before the Committee on Aging, Connecticut General Assembly, February 5, 2013. Available at <u>http://www.ctvoices.org/sites/default/files/02052013_aging_hb5764_nonparentTF A.pdf</u>.

Feder, K.A. "Testimony Regarding Gun Violence Prevention." Hearing before the Gun Violence Prevention Working Group, Bipartisan Task Force on Gun Violence Prevention and Children's Safety, Connecticut General Assembly, January 28, 2013. Available at <u>http://www.ctvoices.org/sites/default/files/012813_sandyhooktaskforce_gunviole</u> <u>nce.pdf</u>

Blog Posts

- Feder, K.A. "When Families Move to Higher Opportunity Neighborhoods, Their Children have Higher Income." *Connecticut Voices for Children*. May 20, 2015. Available at <u>http://www.ctvoices.org/blog/20150520/when-families-move-higher-opportunity-neighborhoods-their-children-have-higher-income</u>.
- Feder, K.A. & Iverson, S. "Connecticut's Students of Color and Low-Income Students are Segregated in Under-Resourced Schools." *Connecticut Voices for Children*. March 11, 2015. Available at <u>http://www.ctvoices.org/blog/20150311/connecticuts-students-color-and-lowincome-students-are-segregated-under-resourced-sch</u>.
- Feder, K.A. "Keeping Kids in the Budget Part 3: Invest Now or Pay Later." *Connecticut Voices for Children*. February 4, 2015. Available at http://www.ctvoices.org/blog/20150204/keeping-kids-budget-part-3-invest-now-or-pay-later.
- Feder, K.A. "Keeping Kids in the Budget Part 2: Long-Term Budget Challenges Put Kids at Risk." Connecticut Voices for Children. February 3, 2015. Available at <u>http://www.ctvoices.org/blog/20150203/keeping-kids-budget-part-2-long-termbudget-challenges-put-kids-risk</u>.
- Feder, K.A. "Keeping Kids in the Budget Part 1: Why are Families Cut First." Connecticut Voices for Children. February 2, 2015. Available at <u>http://www.ctvoices.org/blog/20150202/keeping-kids-budget-part-1-why-are-families-cut-first.</u>
- Feder, K.A. "A Better Measure of Poverty in Connecticut and its Lessons." Connecticut Voices for Children. October 17, 2014. Available at <u>http://www.ctvoices.org/blog/20141017/better-measure-poverty-connecticut-andits-lessons</u>.
- Feder, K.A. "More Should Be Done to Support Educational Success for Children in Foster Care." Connecticut Voices for Children. September 24, 2014. Available at <u>http://www.ctvoices.org/blog/20140924/more-should-be-done-support-</u> educational-success-children-foster-care.

Feder, K.A. "Video Highlights: Helping Children in Foster Care Transition to Adulthood." *Connecticut Voices for Chidlren*. March 6, 2013. Available at <u>http://www.ctvoices.org/blog/20130306/video-highlights-helping-children-foster-care-transition-adulthood</u>

Symposia Organized

Connecticut Voices for Children's 3rd Annual Youth at the Capitol Day Forum: Raising the Grade – Improving Educational Opportunities for Youth in State Care. Held January 16th at the Connecticut State Capitol. Full video available through CT-N at <u>http://ct-n.com/ctnplayer.asp?odID=9814</u>.

Connecticut Voices for Children's 2nd Annual Youth at the Capitol Day Forum: Success Beyond 18 – A Conference Exploring Opportunities and Services for Older Youth in Connecticut's Department of Children and Families. Held December 6th at the Connecticut State Capitol. Abridged video available at <u>http://www.ctvoices.org/events/2012/success-beyond-18-conference-exploring-opportunities-and-services-older-youth-connecticu.</u>