8-2019

Impact of Adverse Childhood Experiences on Mental Health Outcomes and Related Prescription Practices in a Psychiatric Inpatient Sample

Carrie LeMay
East Tennessee State University

Impact of Adverse Childhood Experiences on Mental Health Outcomes and Related Prescription Practices in a Psychiatric Inpatient Sample

---

A dissertation

presented to

the faculty of the Department of Psychology

East Tennessee State University

In partial fulfillment

of the requirements for the degree

Doctor of Philosophy in Psychology,

concentration in Clinical Psychology

---

by

Carrie LeMay

August 2019

Jill Stinson, Ph.D., Chair

Julia Dodd, Ph.D.

Matt Palmatier, Ph.D.

Stacey Williams, Ph.D.

Keywords: Adverse Childhood Experiences, polypharmacy, forensic, psychiatric hospitalization

ABSTRACT

Impact of Adverse Childhood Experiences on Mental Health Outcomes and Related Prescription Practices in a Psychiatric Inpatient Sample

by

Carrie LeMay

A definitive association between adverse childhood experiences (ACEs) and negative physical and mental health outcomes has been established. There is evidence that individuals in forensic psychiatric facilities are disproportionately exposed to ACEs, which may impact severity, prognosis, and age of onset of psychiatric symptoms, including behavioral concerns of institutional aggression, self-harm behaviors, and suicide attempts. Such psychiatric and behavioral concerns are often managed through multiple psychotropic prescriptions, leading to psychotropic polypharmacy. This study evaluated the relationship between ACEs, mental health and behavioral concerns, and psychotropic polypharmacy through analysis of archival data from a forensic inpatient psychiatric facility. A total of 182 patients met inclusion criteria. Through a comprehensive record review, ACE scores, mental health outcomes, behavioral concerns, and prescription practices were ascertained and subjected to a series of regression analyses. Results indicate that the current participants experience greater prevalence of ACEs and mental health outcomes, as well as higher rates of psychotropic polypharmacy. These relationships are mediated by history of self-harm behaviors. The higher polypharmacy rates yield greater negative side effects with the need to manage with additional medications. Taken as a whole, ACEs are a relevant consideration, as childhood adversity may lead to a lifetime of difficulty with managing emotional distress and symptoms of psychopathology. Pharmacological treatment may be necessary, particularly with those who experience more complex mental health

outcomes. However, a primary focus on psychotropic intervention can result in high rates of medications and polypharmacy with significant side effects. Incorporation of non-pharmacological intervention should be a primary consideration with forensic inpatients to circumvent the potential for psychotropic polypharmacy and related negative consequences.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

Adverse Childhood Experiences

Adverse Childhood Experiences (ACEs) describe occurrences of abuse, neglect, and household dysfunction during childhood and adolescence. Childhood abuse and neglect are a significant burden to children and adolescents around the world, with ranging rates of reported emotional abuse (11-47%), physical abuse (14-55%), sexual abuse (6-22%), emotional neglect (15-40%), and physical neglect (7-19%) (Stoltenborgh, Bakermans-Kranenburg, Alink, & van Ijzendoom, 2015). However, ACEs are not confined to only these forms of maltreatment. Ongoing ACE study research has defined ten different types of childhood adversities, additionally including parental separation or divorce, domestic violence in the household, and household member substance abuse, mental illness, and incarceration (Centers for Disease Control; CDC, 2013; Felitti et al., 1998).

Historically, research has emphasized the impact of singular events of trauma or maltreatment on long-term outcomes. Little was known of the impact of cumulative adversity on adult physical and mental health outcomes until the initial ACE survey research. The original study focusing on ACEs (Felitti et al., 1998), as well as a second wave of data collection (CDC, 2013), was conducted from 1995 to 1997 by Kaiser Permanente at their Health Appraisal Clinic in San Diego by examining patients and their medical records. Their purpose was to examine factors related to health outcomes, health care utilization, and causes of death. After medical evaluation, 17,337 patients completed a questionnaire that specifically assessed a range of factors, of which the most important were 10 specific indicators of childhood maltreatment and family dysfunction (i.e., verbal/emotional, physical, and sexual abuse; emotional and physical

neglect; domestic violence in the household; parental separation or divorce; and household member substance abuse, mental illness, and incarceration (CDC, 2013; Felitti et al., 1998). Results from over nine thousand patients revealed that just over half of participants reported experiences of one or more adversities, while 6.2% reported four or more (Felitti et al., 1998). Results from two combined waves of collection showed that over two thirds of respondents endorsed at least one ACE, and one in five reported three or more (CDC, 2013). Felitti et al. (1998) found significant associations between ACEs and numerous medical conditions, including self-reported fair or poor health, chronic obstructive pulmonary disease, diabetes, heart disease, cancer, stroke, hepatitis, and skeletal fractures. ACEs were additionally linked to various health risk factors, such as depression, suicide attempts, sedentary lifestyle, obesity, smoking, alcoholism, intravenous and illicit drug use, and having fifty or more sexual partners (Felitti et al., 1998).

Examining outcomes using ACE survey methodology has advanced our understanding of the impact of cumulative childhood adversity across the lifespan. The more ACEs an individual experiences, the greater their decline in functioning across various domains (Mersky, Topitze, & Reynolds, 2013). These high risk behaviors further contribute to negative physical and mental health outcomes (CDC, 2013). Collectively, ACE research indicates that the impact of ACEs on long-term adult physical and mental health is additive and exponential, meaning, as the number of ACEs to which an individual is exposed increases, the risk for and occurrence of health related problems also increases.

Common interventions for both physical and mental health problems include pharmacology, especially as health issues compound. As a medication regimen becomes more complex, as might be showcased by an individual diagnosed with both physical and mental

health problems or co-morbid mental illnesses, the risk for negative consequences, including drug interactions, side effects, and even death, increases. Yet these potential consequences are often misunderstood, overlooked, or ignored in the pursuit of treating specific conditions and related symptoms (Rambhade, Chakarborty, Shrivastava, Patil, & Rambhade, 2012).

Only limited research describing associations between ACEs, health outcomes, and polypharmacy is available. Further, no published studies to date have examined these relationships in forensic and inpatient mental health populations, despite the evidence that these populations are disproportionately exposed to maltreatment and household dysfunction in childhood, frequently have higher rates of physical and mental health problems, and are usually treated with multiple forms of medications in response to health and behavioral needs. To address gaps in existing research, the relationship between adverse childhood experiences, health outcomes, and prescription practices will be examined within a forensic inpatient setting.

Below, I will discuss the impact of adverse childhood experiences on health outcomes in community, offender, and psychiatric settings. Additionally, definitions of polypharmacy, associated polypharmacy practices, and the potential benefits and risks of these medication regimens will be reviewed.

Childhood Adversity and Health Outcomes

Previous literature has definitively linked experiences of childhood trauma and household dysfunction with health risk behaviors and negative physical and mental health outcomes. These associations are briefly described below.

Health Risk Behaviors

Persons exposed to maltreatment and adversity in childhood are at increased risk of engaging in behaviors in adolescence and adulthood that put their health at risk (Draper et al.,

2008). These health-risk behaviors impact the development and course of physical and mental illness (Felitti, 2009; Mersky et al., 2013). Research links ACEs to such health-risk behaviors as drinking alcohol (Bellis, Lowey, Leckenby, Hughes, & Harrison, 2014; Mersky et al., 2013), smoking tobacco (Anda et al., 1999; Campbell, Walker, &Egede, 2016; Ford et al., 2011; Walsh & Cawthon, 2014), using intravenous and illicit drugs (Allem, Soto, Baezconde-Garbanati, & Unger, 2015; Dube, Felitti, Dong, Chapman, Giles, & Anda, 2003; Mersky et al., 2013; Wu, Schairer, Dellor, & Grella, 2010), physical inactivity (Bellis et al., 2014) and high-risk sexual activity (Bellis et al., 2014). Engaging in these types of risky behaviors is more likely to occur earlier and more frequently with increasing exposure to childhood trauma and household dysfunction (Bellis et al., 2014; Marie-Mitchell & O'Connor, 2013). Increased exposure to ACEs and related health-risk behaviors has also been shown to lead to such things as teenage pregnancy (CDC, 2013), preterm birth (Christiaens, Hegadoren, & Olsen, 2015) and sexually transmitted diseases (Wilson & Widom, 2008), as well as developing alcohol (Dube et al., 2006; Pilowsky, Keyes, & Hasin, 2009) and substance dependence (Bellis et al., 2014; Douglas et al., 2010).

Physical Health Outcomes

Exposure to childhood adversity has been linked to poor self-rated health (Felitti et al., 1998; Mersky et al., 2013) and a variety of physical health outcomes, many of which are mediated by the presence of health-risk behaviors. These forms of morbidity include various forms of cardiovascular disease, liver disease, obesity, diabetes, emphysema, chronic obstructive pulmonary disease, asthma, stroke, cancer, hepatitis, autoimmune disease, fibromyalgia, skeletal fractures, chronic headaches, chronic pain, and irritable bowel syndrome (Anda, Brown, Dube, Bremner, Felitti, & Giles, 2008; Anda, Tietjen, Schulman, Felitti, & Croft, 2010; Bellis et al.,

2014; Campbell et al., 2016; Chartier & Walker, 2009; Danese & Tan, 2014; Dube, Fairweather, Pearson, Felitti, Anda, & Croft, 2009; Dong, Dube, Felitti, Giles, & Anda, 2003; Dong et al., 2004; Felitti et al., 1998; Gilbert et al., 2015; Gunstad et al., 2006; Mersky et al., 2013). As a result, exposure to cumulative ACEs has also been associated with premature death and mortality (Brown et al., 2010; Kelly-Irving et al., 2013). With the exception of smoking tobacco, Brown and colleagues (2009) concluded that the relationship between ACEs, engagement in health-risk behaviors, and diagnosis of several chronic diseases have a modest relationship, with evidence suggesting stronger associations with higher-end ACE scores.

Mental Health Outcomes

The strongest associations between ACEs and adult outcomes relate to mental health concerns (Brown et al., 2009). Similar to physical health outcomes, ACEs have a cumulative negative impact on mental health (Mersky et al., 2013), with higher ACEs associated with greater frequency of self-reported mental distress and psychopathology (e.g., Anda et al., 2005; Chapman, Dube, & Anda, 2007; Chapman, Whitfield, Felitti, Dube, Edwards, & Anda, 2004; Gilbert et al., 2015). ACEs play a key role in the development of specific psychopathologies, such as anxiety (Benjet, Borges, & Medina-Mora, 2010), phobias (Spinhoven et al., 2010), post-traumatic stress disorder (Brockie, Dana-Sacco, Wallen, Wilcox, & Campbell, 2015), sleep disorders (Kajeepeta, Gelaye, Jackson, & Williams, 2015), hallucinations (Whitfield, Dube, Felitti, & Anda, 2005), psychosis (Anda, Brown, Felitti, Bremner, Dube, & Giles, 2007; Koskenvuo & Koskenvuo, 2015; Varese et al., 2012), personality disorders (Afifi et al., 2011), autobiographical memory disturbances (Edwards, Fivush, Anda, Felitti, & Nordenber, 2001), problematic substance use (Benjet et al., 2010; Brockie et al., 2015), mood disorders (Benjet et al., 2010; Mersky et al., 2013) and depression (Brockie et al., 2015; Chapman et al., 2004;

Spinhoven et al., 2010), as well as suicidal ideation (Turner, Finkelhor, Shattuck, & Hamby, 2012) and suicidal behaviors (Bellis et al., 2014; Brockie et al., 2015; Dudeck et al., 2016).

ACEs have been additionally associated with externalizing problems, including antisocial behavior (Schilling, Aseltine Jr., & Gore, 2007; Reavis, Looman, Franco, & Rojas, 2013), interpersonal violence and aggression (Duke, Pettingell, McMorris, & Borowsky, 2010; Odgers et al., 2008), juvenile delinquency (Fox, Perez, Cass, Baglivio, & Epps, 2015), impulsivity (Duke, Pettingell, McMorris, & Borowsky, 2010), and attention deficit hyperactivity disorder (Brown, Brown, Briggs, German, Belamarich, & Oyeku, 2016; Fuller-Thomson & Lewis, 2015).

ACEs in Forensic Mental Health Patients

Research indicates that as a person is exposed to childhood adversity, their likelihood for experiencing more than one of the aforementioned physical or mental illnesses also increases, even after controlling for health-risk behaviors and other psychosocial factors (Sinnott, McHugh, Fitzgerald, Bradley, & Kearney, 2015); however, a great majority of the studies evidencing this relationship have examined only community samples. Relatively few studies have been conducted in psychiatric or forensic populations, despite evidence that these populations are disproportionately exposed to childhood abuse, neglect, and household dysfunction (Baglivio, Epps, Swartz, Sayedul Huq, Sheer, & Hardt, 2014; Rytila-Manninen et al., 2014).

Childhood Adversity and Psychiatric Populations

Research has investigated the relationship between singular types of abuse in childhood and various forms of serious mental illness (e.g., Spidel, Lecomte, Greaves, Sahlstrom, & Yuille, 2010), but only in the last two decades has the cumulative impact of childhood maltreatment and household dysfunction been considered. Total ACE score has been associated with serious mental illness diagnosis (Sacco, Head, Vessicchio, Easton, Prigerson, & George, 2007). In a

review, Grubaugh and colleagues (2011) reported that 90% of adults with serious mental illness have experienced at least one adverse experience in childhood. One study found that 46% of individuals with serious mental illness reported experiencing at least three ACEs (Rosenberg, Lu, Mueser, Jankowski, & Cournos, 2007), while another study reported that 38.9% of people with serious mental illness reported four or more childhood adversities (Stumbo, Yarborough, Paulson, & Green, 2015).

Experiencing adversity earlier in life, particularly during childhood, may lead to earlier onset of mental health problems (McLaughlin, Green, Gruber, Sampson, Zaslavsky, & Kessler, 2010; Schalinski, Teicher, Nischk, Hinderer, Muller, & Rockstroh, 2016) and more severe psychiatric symptoms in adulthood (Schalinski et al., 2016; Stumbo et al., 2015; Varese et al., 2012). In an examination of psychiatric inpatients, Schalinski and colleagues (2016) reported that 89.8% met criteria for one or more ACEs, with an overall average of three childhood adversities and 37% exposed to at least four. Additionally, examining depression, dissociation, and PTSD symptom severity, researchers concluded that the factors most predictive of symptom severity were age of exposure (depression, dissociation, PTSD), duration of exposure (depression), overall severity of exposure (PTSD), and total number of childhood adversities to which a patient was exposed (PTSD and dissociation; Schalinski et al., 2016).

Childhood Adversity and Offender Populations

Evidence describing childhood adversity within forensic samples has primarily originated from juvenile and adult offender populations. Research demonstrates that childhood abuse and household dysfunction are more common among criminal offenders comparated to non-offenders (Levenson, 2013). In a study of juvenile offenders, Baglivio and colleagues (2015) found only a small percentage of adolescent male (3.1%) and female (1.8%) offenders reporting no ACEs,

while those who reported one experience of childhood adversity were more likely to report additional ACEs. Additionally, these juvenile offenders were four times more likely to have experienced four or more ACEs than those in the original ACE survey research that utilized community samples (Baglivio et al., 2015). Examining the effects of ACEs on psychiatric disorders in adolescent male offenders, Beilas and colleagues (2015) found that 91.5% of participants reported experiencing at least one ACE, and 75% reported two or more. In their study of chronic violent juvenile offenders, Fox and colleagues (2015) found that after controlling for criminal behavior and other risk factors, each additional adversity experienced as a child increased the risk of becoming a serious, violent, and chronic juvenile offender by 35 percent.

Similar relationships are shown in adult offender populations. In one examination of childhood adversity, 30.7% of inmates reported exposure to four or more ACEs (Messina, Grella, Burdon, & Pendergast, 2007). Another study comparing four offender groups – nonsexual child abusers, sexual offenders, domestic violence offenders, and stalkers – reported that offender groups experienced nearly four times as many adverse events in childhood than the male normative sample, and that experiencing four or more events was reported at significantly higher levels among a criminal population (Reavis et al., 2013). In their study comparing male sexual offenders to a CDC community sample, Levenson, Willis, and Prescott (2014) found that nearly half of the offender sample reported at least four ACEs and were significantly more likely to endorse each of the ten ACE categories.

Female offenders exhibit results similar to their male offender counterparts. When compared to a female community sample, female sexual offenders were found to have reported experiencing no ACEs at significantly lower rates and being exposed to at least four adverse

events at significantly higher rates (Levenson, Willis, & Prescott, 2015). Additionally, Levenson and colleagues (2015) determined that female offenders were more likely to have experienced specific childhood adversities (e.g., three times more likely to have experienced emotional neglect, sexual abuse, and have household member incarcerated during childhood or adolescence) compared to females in a community sample.

Behavioral characteristics associated with offender populations (e.g., violence) and psychopathology, as well as their relationship to childhood adversity, have also been examined in offender populations. ACEs have been associated with reduced adaptability and increased social isolation, reduced self-esteem, and increased rates of dissociation and anger (Monnat & Chandler, 2015), as well as antisocial tendencies (Odgers et al., 2008). Among male adolescent offenders, cumulative ACE score is predictive of such psychopathology as PTSD, anxiety disorders, depressive disorders, and suicidality (Bielas et al., 2016). In a study investigating the relationship between adverse childhood events and types of aggressive behavior in adolescent males, Duke and colleagues (2010) found that for each ACE identified, there was an increased risk of violence among participants.

The association between childhood adversity and violence has been examined in adult populations as well, demonstrating a clear link between violent behaviors and experiences of childhood adversity (CDC, 2016; Hilton, Ham, & Green, 2016). One study identified three specific adverse events (i.e., physical abuse, sexual abuse, household violence toward the mother) to be associated with the perpetration of intimate partner violence. Those males who experienced all three events were four times as likely to repeatedly engage in intimate partner violence as adults (Whitfield, Anda, Dube, & Felitti, 2003).

Childhood Adversity and Forensic Mental Health Populations

Comparative to research examining offender and psychiatric populations, studies examining the prevalence of ACEs and their relationship to associated factors in forensic psychiatric inpatient samples are minimal. One study that examined six categories of adverse childhood experiences in a forensic mental health sample reported higher rates of adversity compared to a community sample, in which approximately three-fourths of patients reported experiences of at least one type of childhood maltreatment, just over half reported two or more, and nearly one-fifth reported four or more forms of childhood adversity (Stinson, Quinn, & Levenson, 2016).

While little research has examined the prevalence and possible impact of cumulative ACEs in forensic psychiatric inpatient populations, some research has suggested high prevalence rates of specific childhood traumas. For example, Beck and colleagues (2017) reported that almost 90% of adult female forensic psychiatric inpatients classified as highly aggressive had experienced physical or sexual abuse as a child. Notably, individuals in this group had experienced the onset of psychiatric symptoms by the age of twelve (Beck et al., 2017).

Dudeck and colleagues (2016) examined the relationship between ACEs, suicide attempts, and appetitive aggression, defined as perpetration of violence for the purpose of enjoyment, in 55 male forensic psychiatry inpatients. Results indicated that 34% of patients reported no ACEs, while 17% reported experiencing five or more adverse events in childhood. Additionally, these researchers reported ACEs as well as appetitive aggression to be predictors of suicidal behavior (Dudeck et al., 2016).

In their study examining the impact of childhood adversity on mental illness and aggressive and criminal behaviors in 381 forensic mental health inpatients, Stinson and

colleagues (2016) reported that 92.4% of patients met criteria for at least two psychiatric disorders. Cumulative adversity scores were associated with younger ages of first arrest, psychiatric hospitalization, and onset of aggressive behavior. Additionally, 36.6% of patients had a history of attempting suicide, and 38.4% had a history of non-suicidal self-injurious behaviors. As cumulative adversity scores increased by one, patients were 22.4% more likely to have a combined history of suicide attempt and/or self-injurious behaviors. However, despite the strength of these relationships between ACEs and psychiatric and criminal outcomes, it was also noted that the addition of foster care placement diminished the predictive strength of the ACE score itself (Stinson et al., 2016).

Intervention Practices in Forensic Mental Health Populations

A significant focus of research examining forensic inpatient populations has been the use and effectiveness of varied interventions. In a systematic review (Tapp, Perkins, Warren, Fife-Shaw, & Moore, 2013), researchers examined dietary, neurophysiological, psycho-educational, behavioral, psychological, and pharmacological interventions. The perhaps most commonly used interventions were pharmacological in nature. Examination of pharmacological interventions predominantly involves the use of antipsychotic medications for persons with treatment-resistant schizophrenia. While several studies provided evidence to support the use of antipsychotics and other medications to manage psychiatric symptoms as well as aggression, most had identifiable methodological restrictions that prevented a determination of treatment effectiveness (Tapp et al., 2013).

Because of the comparatively high prevalence rates of childhood adversity within forensic inpatient populations, it is likely that prominent psychiatric and behavioral symptoms are impacted by the presence of early trauma and maltreatment. Because mental health and

behavior management are a primary goal of forensic inpatient facilities, understanding medication practices and their relationship to specific behaviors, diagnoses, and precipitating factors is vital. Patients residing within forensic mental health inpatient facilities reportedly experience comparatively higher rates of childhood maltreatment and household dysfunction, thus potentially impacting the severity, prognosis, and age of onset of psychiatric symptoms. Higher rates of co-morbid and serious mental illness are found within this population. Pharmacotherapy has been identified as a primary treatment for serious mental illness (Tapp et al., 2013), and management of mental illness is frequently maintained through multiple prescriptions (Kukreja, Kalra, Shah, & Shrivastava, 2013). As such, these patients often receive multiple psychotropic medications as a primary treatment. It is necessary to gain a better understanding of medication practices, particularly polypharmacy, and the relationship to these diagnoses.

Polypharmacy

Polypharmacy is defined within the empirical literature in varying ways, with the broadest definition referring to a single patient using multiple medications concurrently. However, even within this definition, the majority of research does not specify what qualifies as a "medication" beyond the generalized term of "drug," or when discussing a specific drug or class of drugs (i.e., antipsychotic medications). One study included prescriptions, over the counter drugs, vitamins, and supplements under the umbrella definition of "medication" (Leahy, 2017).

Polypharmacy has been defined quantitatively, qualitatively, and by the disease states for which prescriptions are given (i.e., psychotropic polypharmacy). Quantitatively it has been defined as ranging from two or more medications taken by one person (Cosano et al., 2016;

Dwyer, Han, Woodwell, & Rechtsteiner, 2010; Gniidic, Tinetti, & Allore, 2017; Guthrie, Makubate, Hernandez-Santiago, & Dreischulte, 2015; Haider, Johnell, Weitoft, Thorslund, & Fastborn, 2009; Janssen, Weinmann, Berger, & Gaebel, 2004; Jokanovic, Tan, Dooley, Kirkpatrick, & Bell, 2016; Jyrkka, Enlund, Korhonen, Sulkava, & Hartikainen, 2009; Leahy 2017; Naples & Haiiar, 2016; Millan, 2014; Preskon & Lacey, 2007; Scott et al 2015; Viktil, Blix, Moger, & Reikvam, 2007; Vyas, Pan, Sambamoorthi, 2012). Others define polypharmacy qualitatively to include if a medication is prescribed without clinical indication, when an ineffective medication continues to be prescribed, if therapeutic duplication is present (Naples & Haiiar, 2016), and if a medication is used to treat a side effect or secondary symptom of another medication from a different drug class (de las Cuevas & Sans, 2005).

Polypharmacy within drug classes has been defined separately, with the most common definition referring to two or more medications of the same drug class being prescribed simultaneously (Cuevas & Sans, 2005; Londono et al., 2016). For example, psychotropic polypharmacy can refer to prescribing an anti-depressant and a mood stabilizer. More specifically, antipsychotic polypharmacy refers to the prescription of two or more antipsychotic medications (e.g., clozapine and olanzapine).

Regardless of definition, the prevalence of polypharmacy continues to rise (Alpert, 2015). Increasing rates of polypharmacy are driven by a culture of single condition, guideline-driven prescribing practices and an increased prevalence of physical multimorbidity and psychological co-morbidity. Recent clinical guidelines have focused on the treatment of single conditions, which fail to account for these growing rates of multimorbidity (Moriarty, Hardy, Bennett, Smith, & Fahey, 2015). Additionally, professional guidelines recommend treatment of disease and illness with multiple drugs to achieve positive outcomes (Guthrie, Makubate, Hernandez-

Santiago, & Dreischulte, 2015). And while polypharmacy drug regimens can have positive benefits, the practice may also result in severe negative consequences.

Clinical Consequences of Polypharmacy

Positive Consequences

Polypharmacy often carries a negative connotation; however, in some cases it can be appropriate, such as when treating physical multimorbidity or serious mental illness. With regard to treating psychopathology and the potential benefit of polypharmacy, a great majority of the research has focused on psychotropic polypharmacy, though few studies evaluate psychotropic polypharmacy beyond antipsychotic polypharmacy. Most psychotropic polypharmacy research reports on the prevalence within populations with serious mental illness but seldom measure effectiveness. Peselow and colleagues (2016) compared pharmacological monotherapy management of bipolar disorder to polypharmacy management, with results indicating that patients experience greater symptom stability when pharmacotherapy management included two or more psychotropic medications. Some research supports the use of antipsychotic polypharmacy in treating those with schizophrenia resistant to monotherapy (e.g., Morrissette & Stahl, 2014). Additionally, antipsychotic polypharmacy has been proposed to mediate and decrease certain types of violence (e.g., Stahl, 2014); however, most antipsychotic polypharmacy research emphasizes the risk of polypharmacy and advises against its use.

Negative Consequences

The inherent complexity of treating co-morbid chronic illnesses and psychological disorders may be effectively addressed through polypharmacy; however, treatment must be carefully monitored due to the overwhelming conclusions of polypharmacy research that emphasize the negative clinical consequences of multiple drug regimens. The number of

medications a person is taking is the single most important predictor of harm (Scott et al., 2015). Each drug added to a patient's medication regimen increases the likelihood of adverse outcomes (Preskorn & Lacey, 2007). The presence of one medication can alter the nature, magnitude, or duration of the effect of another medication by influencing the drug's metabolism, absorption, and distribution within the body (Preskorn & Lacey, 2007). Polypharmacy has been consistently identified as a risk factor for increased adverse drug reactions, drug-drug interactions, cost of care, medication regimen nonadherence, inappropriate prescribing, functional impairment, morbidity, mortality, and, specific to antipsychotic polypharmacy, extrapyramidal side effects. Studies show an association between the number of medications a person is taking and linear increases in negative health outcomes (Fried, O'Leary, Towle, Goldstein, Trentalange, & Martin, 2014), even when only by one medication (Leahy, 2017). Factors particularly relevant to forensic inpatient populations, many of whom may require complex medication regimens, will be described below.

Adverse drug reactions. Drug-related problems and adverse drug events are regularly reported as direct consequence of polypharmacy practices (Viktil et al., 2006). An adverse drug event (ADE) is defined as injury resulting from medication (Naples & Hajjar, 2016) that includes adverse drug reactions, medication errors, allergic reactions, and drug overdoses. ADEs are becoming increasingly common and account for a significant percentage of healthcare utilization (ODPHP, 2017). ADEs have become larger contributors to outpatient and emergency room visits (Burgess, Holman, & Satti, 2005) and as the primary cause for hospitalization (Bourgeois, Shannon, Valim, & Mandl, 2010).

Adverse drug reactions (ADR), defined as noxious and unintended responses that occur at a normal dose of medication, are the most common type of ADE (Naples & Hajjar, 2016). As

the number of medications taken increases, the risk of ADRs increases (Leahy, 2017). For example, outpatients had an 88% higher risk of ADRs when taking five or more medications (Bourgeois et al., 2010). Similarly, compared to those taking fewer medications, hospitalized older adults taking five or six medications or those taking seven or more medications were two and four times as likely to experience an ADR, respectively (Onder et al., 2010).

The most common complications resulting from ADRs include gastrointestinal complications, metabolic and hemorrhagic complications, and sedation (Armstrong & Temmingh, 2017; Barnes & Paton, 2011; Medeiros-Souza, dos Santos-Neto, Kusano, & Pereira, 2007). The consequences of ADRs can be severe, potentially leading to hospitalization and even death (Medeiros-Souza et al., 2007; Naples & Hajjar, 2016). In their population-based analysis of changes in polypharmacy and related interactions, Guthrie and colleagues (2015) identified cardiovascular, central nervous system, gastrointestinal, and endocrine drug classes as seeing the largest absolute rise. Many drugs most commonly associated with ADRs, including cardiovascular drugs, diuretics, nonsteroidal anti-inflammatory drugs, agents to address diabetes, anticoagulants, antibiotics, anticonvulsants, and antipsychotics are classified in these groups (Medeiros-Souza et al., 2007; Naples & Hajjar, 2016). Still, the two drug classes most commonly associated with negative side effects are cardiovascular drugs and those specific to the central nervous system, like benzodiazepines (Medeiros-Souza et al., 2007).

Drug-drug interactions. Polypharmacy is associated with higher rates of drug-drug interactions (DDIs; Guthrie et al., 2015). DDIs occur when two or more drugs react with one another. These interactions may increase or decrease the effectiveness of a medication or cause negative side effects, such as sedation (Food and Drug Administration, 2016). These interactions are a frequent cause of preventable ADEs (Naples & Hajjir, 2016).

As the number of drugs prescribed increases, the likelihood for potentially serious DDIs escalates. For example, the proportion of people with potentially serious DDIs was 80.8% among those prescribed 15 or more medications, compared to 10.9% of those prescribed 2 to 4 medications (Guthrie et al., 2015). Similarly, in a study of older adults, it was determined that the probability of DDIs increased 50% when prescribed five to nine medications and 100% when 20 or more medications were prescribed (Doan, Zakrewski-Jakubiak, Roy, Turgeon, & Tannenbaum, 2013). Additionally, the proportion of the population at risk for serious DDIs more than triples, regardless of age group, because of polypharmacy (Guthrie et al., 2015).

Cost of care. Each drug added to a medication regimen not only increases the likelihood of adverse outcomes but also the expense of treatment (Preskorn & Lacey, 2007). Inappropriate polypharmacy has high associated costs for patients, insurance companies, and the government (Anda, Brown, Felitti, Bremner, Dube, & Giles, 2007; Viktil et al., 2006). Increased costs are attributable to increased cost of prescriptions, new drug development, and increases in prescribing practices (Medeiros-Souza et al., 2007). The latter factor not only increases cost due to the number of prescriptions but also because of the increased costs associated with the higher risk of ADEs.

In a study of antipsychotic polypharmacy among 246 state hospital male inpatients, Lacassee (2014) demonstrated an association between antipsychotic polypharmacy and length of stay. Interestingly, a majority of patients were either admitted already on or subsequently given antipsychotic polypharmacy regimens (Lacassee, 2014). Researchers insist that antipsychotic polypharmacy not only tends to result in high dosing (Gallego, Bonetti, Zhang, Kane, & Correll, 2012), but it also impairs functional recovery (Wunderlink, Nieboer, Wiersma, Sytema, & Nienhuis, 2013) and can lead to extended hospitalization (Lacassee, 2014).

Extrapyramidal side effects. Potentially serious adverse effects can stem from first generation antipsychotic and antipsychotic polypharmacy prescriptions (Armstrong & Temmingh, 2017). In a population-based study, Carnahan and colleagues (2006) reported that compared to patients receiving antipsychotic monotherapy, those receiving antipsychotic polypharmacy were at an increased risk of being prescribed medications meant to treat extrapyramidal side effects. These extrapyramidal side effects, or drug induced movement disorders, include dystonia, akathisia, Parkinsonism, and tardive dyskinesia (Buckley, Citrome, Nichita, & Vitacco, 2011; Pierre, 2005).

These types of side effects often discourage patient willingness to maintain prescribed medication regimens, not only because of the related symptoms but also because many medications prescribed to counteract extrapyramidal side effects have negative side effects of their own (Carnahan, Lund, Perry, & Chrischilles, 2006). The most commonly recommended medications to treat extrapyramidal side effects are anticholinergics, less commonly, dopamine agonists. (Pringsheim, Doja, Belanger, & Patten, 2011). Because atypical antipsychotics have varying degrees of anticholinergic effects, adding an anticholinergic drug yields a potential for serious side effects that cause physical and mental deterioration, which can significantly impair overall functioning. Potential side effects may include sedation, memory impairment, constipation, blurry vision, and confusion (Lieberman, 2004), with a majority of research investigating effects of anticholingeric drugs linking cognitive impairment and eventual dementia (Campbell et al., 2009).

Mortality. Polypharmacy has been associated with an increased risk of mortality (Lacassee, 2014). Research indicating increased mortality as a consequence of polypharmacy largely focuses on older adult populations and patients taking multiple antipsychotic

medications. For example, in one study of older adults in Spain, polypharmacy of six or more medications was associated with a nearly two-fold increase in mortality risk (Gomez, Vega, Bermejo-Pareja, Medrano, Louis, & Benito-Leon, 2014). In a review of antipsychotic polypharmacy, Langan and Shajahan (2010) concluded that antipsychotic polypharmacy is an increasing concern due to evidence that the more antipsychotics given concurrently, the shorter a patient's lifespan (e.g., Waddington, Yousseff, & Kinsella, 1998). Additionally, one study reported a graded relationship between mortality and the number of neuroleptics prescribed, noting that those prescribed three antipsychotics were twice as likely to die than those prescribed only one (Joukamaa, Heliovaara, Knekt, Aromaa, Raitasalo, & Lehtinen, 2006). Generally, research has indicated that mortality is not dependent on average daily dose or total lifetime dose of antipsychotic medications, but rather the maximum number of antipsychotic medications a patient takes concurrently (NASMHPD, 2001).

Polypharmacy and ACEs

The available literature suggests a relationship between ACEs and prescription practices. Using data from the original ACE study, Anda and colleagues (2007) found a graded relationship between total ACE score, prescription rates, and prescribing more serious classes of medications, including antidepressants, anxiolytics, antipsychotics, and mood stabilizers. Bjorkenstam and colleagues (2013) reported a similar relationship of increased risk of psychotropic medication use for Swedish participants as their reported ACEs increased. Koskenvuo and Koskenvuo (2014) reported a graded linear relationship between ACEs and psychotropic medication purchase in a Finnish population, with individuals reporting five to six childhood adversities more likely to use psychotropic medications than those who experienced fewer or no adversities. Additionally, those who had experienced conflict within their family during childhood were

twice as likely to use multiple antipsychotics, mood stabilizers, antidepressants, anxiolytics, hypnotics, and sedatives (Koskenvuo & Koskenvuo, 2014).

Although research related to ACEs and polypharmacy is minimal, several studies have focused on the relationship of polypharmacy to other factors associated with ACEs, including lower socioeconomic status and serious mental illness. Individuals in lower socioeconomic groups often experience physical multimorbidity and psychological co-morbidity and, on average, experience negative health outcomes ten to fifteen years earlier than more economically advantaged populations (Guthrie et al., 2015). In their population database analysis examining how the prevalence of polypharmacy changed between 1995 and 2010, Guthrie and colleagues (2015) demonstrated that people living in more deprived areas were more than twice as likely to be prescribed ten or more drugs, even after controlling for age and residence in long-term care facilities.

Polypharmacy and Forensic Mental Health Populations

Given the rates of ACEs in forensic and inpatient mental health populations, it is not surprising that mental illness and psychotropic medication use are prevalent as well. In a review of polypharmacy in psychiatry, Moller and colleagues (2014) reported similarities in the prevalence of polypharmacy among patients in university hospitals, state hospitals, and inpatient psychiatry wings of general hospitals. For example, one study reported no significant difference in the rates of polypharmacy for outpatient (52.1%) and inpatient (44.3%) populations (Karadag, Orsel, & Turkcapar, 2012). Across settings, polypharmacy is increasing, most notably in psychiatric medicine where the occurrence of prescribing more than four psychotropic medications per person has significantly increased in the last two decades (Moller et al., 2014).

Rates of psychotropic polypharmacy differ with regard to treatment of specific psychiatric disorders. In a review of polypharmacy trends associated with bipolar disorder, Fornaro and colleagues (2016) reported psychotropic polypharmacy rates as high as 85%, noting specific antidepressant polypharmacy rates of 45% and antipsychotic polypharmacy rates of 80%. In fact, the most significant increases in psychotropic polypharmacy are associated with antidepressant and antipsychotic medication use (Karadag et al., 2012; Moller et al., 2014).

Despite the widespread practice of antipsychotic polypharmacy in inpatient settings, there is little evidence to support the effectiveness of this practice in addressing schizophrenia-related symptoms in comparison with monotherapy (Mace & Taylor, 2015). Beyond treatment of psychotic symptoms, antipsychotics are also often used to manage actual or perceived violent behavior in those with psychosis, particularly within inpatient forensic settings (Swanson et al., 2008). One study found that while severity of symptoms was similar between male and female inpatients, being male was predictive of antipsychotic polypharmacy (Lacassee, 2014). Lacasse (2014) also concluded that among males who had been previously committed for forensic reasons, their status as forensic referrals may have elicited perceived dangerousness and thus influenced physician prescription practices. Research suggests that using antipsychotic medications for treatment of aggression should be limited due to the risk of serious side effects (Krakowski, 2008; Morrissette & Stahl, 2014; Suokas, Suvisaari, Haukka, Korhonen, & Tiihonen, 2013). Other medications often used to treat violent behaviors with some effectiveness include mood stabilizers, beta-blockers, and antidepressants; however, each of these has only been reported as effective in certain populations, and each carries contraindications for its use (e.g., beta-blockers should not be used in patients with cardiovascular disease, asthma, or diabetes; Krakowski, 2008).

Beyond aggression and violent behaviors, another common concern within inpatient settings is suicidal behavior. In psychiatric hospitals, individuals with suicidal ideation and suicide attempts (Fontanella, Bridge, & Campo, 2009), as well as impulsivity and self-harm behaviors, are frequently treated with psychotropic polypharmacy medication regimens (Madan, Oldham, Gonzalez, & Fowler, 2015). In a study examining the effectiveness of pharmacological interventions for adolescent inpatients with suicidal ideation and behaviors, Fontanella and colleagues (2009) reported the additions of at least one antidepressant, mood stabilizer, or antipsychotic medication in 78% of suicidal patients. Results indicated that treatment with an antidepressant at discharge was associated with a lower risk of hospital readmission, while being discharged with three or more medications of different drug classes was associated with a 2.6 times greater risk of readmission (Fontanella et al., 2009).

Study Overview

While a definitive association between ACEs and negative outcomes has been established, particularly in community samples, little research has examined the relationship between ACEs, related negative outcomes, and psychotropic prescription practices in forensic mental health populations, who experience markedly increased ACEs, serious psychopathology, and polypharmacy.

This study will use a subset of existing data collected within the context of a larger study to address gaps in the literature and achieve the following aims:

- Establish patterns of polypharmacy use across varying diagnostic presentations and with a degree of diagnostic comorbidity;

- Identify relationships between ACEs, demographic factors, aggression, and suicidality/self-harm in forensic mental health patients receiving multiple medications; and
- Examine the impact of these factors on polypharmacy practices, including medical and psychotropic polypharmacy.

In order to meet these aims, eight hypotheses will be tested:

1. Patients with more mental health diagnoses will exhibit a greater degree of psychotropic polypharmacy.
2. Patients with serious mental illness diagnoses will exhibit a greater degree of polypharmacy.
3. Patients with longer length of hospitalization will evidence greater polypharmacy.
4. Regardless of diagnosis, higher ACEs will be predictive of greater polypharmacy use.
5. Demographic factors, including age, gender, and race/ethnicity, will affect polypharmacy use.
6. Patients with a history of ACEs and that have prior histories of self-harm, suicide attempts, institutional aggression, or lengthier occurrences of psychiatric hospitalization will be prescribed a greater number of psychotropic medications.
7. Patients with a history of ACEs and that have prior histories of self-harm, suicide attempts, institutional aggression, or lengthier occurrences of psychiatric hospitalization will experience greater antipsychotic and mood-stabilizing polypharmacy.
8. Higher rates of polypharmacy will yield a greater number of medications prescribed to address pharmacological side effects.

CHAPTER 2

METHODS

Setting and Sample

The current study will use archival data collected from a larger study of ACEs in forensic mental health inpatients residing in a maximum- and intermediate-security forensic hospital in the Midwestern U.S. The research team for this study included a forensic clinical psychologist, an epidemiologist, and trained undergraduate and graduate research assistants.

Data were collected from 2013-2014. Participants were patients admitted to the facility following acts of aggression in the community or other, less secure facilities, and whose charges had subsequently been dropped. Inclusion criteria for participant eligibility included admission to the facility after 2005, discharge prior to data collection, and facility residence of at least one year. Data from a total of 182 residents were obtained. The records of each were reviewed and included within the larger dataset. All procedures were approved by the ETSU Medical IRB and the Research Review Committee of the participating institution and state Department of Mental Health. Data collection was funded by East Tennessee State University through a Research Development Committee Major Grant.

Terms

Polypharmacy

In the current study, polypharmacy is defined as the concurrent prescription of five or more medications. While the literature gives no universally agreed upon or definitive definition of polypharmacy, research has demonstrated that using more than four medications represents an increased potential risk for the occurrence of drug related problems, increased poor health outcomes, and, in many cases, does not improve the clinical efficacy of treatment (Viktil et al.,

2006). Psychotropic polypharmacy will be defined as the use of two or more psychotropic medications concurrently. While definitions within the literature vary from the concurrent use of two to four medications, the most commonly used definition is two or more (Londono et al., 2016).

Measures

Adverse Childhood Experiences (ACE) Survey

Participants' ACE scores were determined from review of patient medical records. The ACE survey (Felitti et al., 1998) is a ten-item measure assessing exposure to various adversities in childhood. Specific adversities measured include emotional abuse, physical abuse, sexual abuse, emotional neglect, physical neglect, parental separation or divorce, domestic violence in the household, incarceration of a household member, household substance abuse, and mental illness in the household, all prior to the participant reaching the age of 18. Each ACE item was coded as either present (1) or absent (0), and the ACE score was determined by summing each of the 10 ACE items.

Procedure

Once participant selection was complete, trained research assistants reviewed archival data from each participant's chart including medical, psychiatric, and social service records, family reports, annual review reports, and discharge summaries. Psychiatric diagnoses were categorized using the DSM-IV-TR diagnostic codes. Diagnoses were collapsed into categories that included mood disorder, psychotic disorder, impulse related disorder, anxiety disorder, attention deficit hyperactivity disorder, sexual disorder, intellectual and developmental disability, and specific personality disorders. For example, diagnoses with a mood specifier (e.g., depression, bipolar disorder) were categorized as mood disorders. The presence of a diagnosis

was coded dichotomously as absent or present. This permitted co-morbidity and diagnostic variability among mental health evaluators (e.g., schizoaffective disorder vs. co-morbid schizophrenia and depression). A history of attempted suicide and self-harm behaviors were dichotomously recorded as absent or present. Aggression was determined through a recorded history of aggression within the community or within any previous or the current institutional setting. Each of these variables were coded dichotomously as absent or present. Prescribed psychotropic medications were categorized by the disease condition they are approved to treat (e.g., antidepressant) and also dichotomously coded as absent or present.

Statistical Analysis Plan

Hypothesis 1

Patients with more mental health diagnoses will exhibit a greater degree of psychotropic polypharmacy. Diagnostic presentation was examined by number of diagnostic categories (e.g., mood disorder, psychotic disorder, anxiety disorder). Polypharmacy was examined in three ways: overall polypharmacy coded dichotomously (no polypharmacy versus polypharmacy), number of medications prescribed, and incidence of polypharmacy of specific classes of drugs (dichotomously coded).

To assess the relationship between diagnostic presentation and polypharmacy use, logistic and Poisson regressions were used. Specifically, logistic regression was used to examine the relationship between diagnostic variable and presence of any type of polypharmacy, as well as between diagnostic variable and specific classes of drugs. Poisson regression analysis was used to examine associations between diagnostic variables and number of medications prescribed.

Hypothesis 2

Patients with serious mental illness diagnoses will exhibit a greater degree of polypharmacy. Serious mental illness (SMI), as defined by a diagnosis of a bipolar or psychotic-spectrum disorder, was examined dichotomously (i.e., diagnosis of at least one SMI versus no SMI diagnosis). Polypharmacy was examined in three ways: overall psychotropic polypharmacy coded dichotomously (no polypharmacy versus polypharmacy), number of medications prescribed, and incidence of polypharmacy for specific classes of drugs (dichotomously coded). Poisson and logistic regression analyses were employed to examine these relationships. Specifically, Poisson regression was used to examine the association between SMI and number of medications. Logistic regression analyses were used to examine the relationships between SMI and the presence of types of polypharmacy (psychotropic, mood stabilizer, antipsychotic).

Hypothesis 3

Patients with longer length of hospitalization will evidence greater polypharmacy. Length of hospitalization was determined by comparing admission and discharge dates. Poisson regression was used to examine the association between length of hospitalization and number of prescribed medications. Logistic regression analyses were used to examine the relationship between length of hospitalization and the presence of each identified type of polypharmacy (psychotropic, mood stabilizer, antipsychotic).

Hypothesis 4

Regardless of diagnosis, higher ACEs will be predictive of greater polypharmacy use. Diagnostic presentation was examined by number of diagnostic categories identified within participants' medical records. ACE score were examined in two ways: total ACE score and ACE score of four or more, coded dichotomously (i.e., less than four ACEs versus four or more

ACEs). Poisson regression was used to examine relationships between ACE variables and number of mental illness diagnostic categories. Additionally, Poisson and logistic regression analyses were used to examine the relationship between ACE variables and psychotropic polypharmacy practice, as defined previously.

Hypothesis 5

Demographic factors, including age, gender, and race/ethnicity, will affect polypharmacy use. Exploratory analyses, including correlations and chi-squares, were used to examine relationships between polypharmacy practices, age, gender (male and female), and race/ethnicity (white and non-white). Gender and race were coded as dummy variables. If significant relationships were identified those relationships were examined with linear regression analysis.

Hypotheses 6 and 7

Patients with prior histories of self-harm, suicide attempts, institutional aggression, or lengthier occurrences of psychiatric hospitalization will be prescribed a greater number of psychotropic medications. Additionally, patients with prior histories of self-harm, suicide attempts, institutional aggression, or lengthier occurrences of psychiatric hospitalization will experience greater antipsychotic and mood-stabilizing polypharmacy. To examine the impact of ACEs, aggression, suicidality/self-harm behaviors, and history of psychiatric hospitalization on varying types of polypharmacy practices, regression and mediation analyses were conducted. To assess the relationship between experiences of childhood adversity and polypharmacy, the impact of ACE scores on number of medications were examined using linear regression analyses. Two linear regression analyses were used to assess the relationship between cumulative ACE score and degree of overall polypharmacy and degree of psychotropic polypharmacy. Logistic regression analyses were used to examine the relationship between cumulative ACE

score and types of psychotropic polypharmacy (i.e., antipsychotic, mood stabilizer, antidepressant polypharmacy).

The relationship between aggression, suicidality, and self-harm behaviors with polypharmacy were examined with three logistic regression and three linear regression analyses examining the impact of aggression, suicidality (operationally defined as history of suicide attempts and dichotomously coded as no history versus history), and self-harm behaviors (defined as history of self-harm, dichotomously coded) on polypharmacy practices (i.e., defined as psychotropic polypharmacy, dichotomously coded) and on the degree of psychotropic polypharmacy (i.e., number of psychotropic medications prescribed). To assess the relationship between history of psychiatric hospitalization and polypharmacy practices, linear and logistic regressions were used. Specifically, logistic regression was used to examine the relationship between history of psychiatric hospitalization (defined by number of previous hospitalizations) and if a patient is or is not on a psychotropic polypharmacy regimen. Linear regression analysis was used to determine if history of psychiatric hospitalization is predictive of the number of psychotropic medications prescribed.

Mediating pathways were additionally examined. Age, gender, and race served as covariates; total ACE score and an ACE score of four or more served as the independent variables; and aggression, suicidality, self-harm behaviors, and history of psychiatric hospitalization served as mediators. Mediation analyses were conducted, with dependent variables that included number of psychotropic medications, presence of psychotropic polypharmacy, presence of polypharmacy with mood stabilizers, and presence of antipsychotic polypharmacy.

Baron and Kenny (1986) have proposed investigating mediation through a series of three simple regression models (Figure 1). This process is particularly relevant for examining mediating relationships with a dichotomous mediator and/or dependent variables. Step one is to establish a significant relationship between the independent and dependent variables (i.e., significant total effect, path c). Step two is to establish a significant relationship between the independent variable and the mediator (i.e., path a). Step 3 is a multiple regression model to establish a significant relationship between the mediator and dependent variable (i.e., path b) while the independent variable is controlled. Step 4 is to establish if the mediator fully or partially mediates the effect of the independent variable on the dependent variable (i.e., significant direct effect, path c'). Full mediation is indicated if a significant relationship between the independent and dependent variables is eliminated when the mediator is controlled. Partial mediation is indicated when the significant relationship between the independent and dependent variables is reduced but not fully eliminated (Baron & Kenny, 1986).

To rescale the logistic regression predictor and mediator coefficients to make them comparable across equations, each was multiplied by the standard deviation of the predictor variable and then divided by the standard deviation of the outcome variable (Kenny, 2013). The binomial variance was estimated with $\pi/3$ (Kenny, 2013; Newsom, 2016). To determine if the mediation effect is statistically significant, a bootstrapping approach was implemented (Adjei & Karim, 2016; Kenny, 2013; Kenny, 2018; Newsom, 2016).

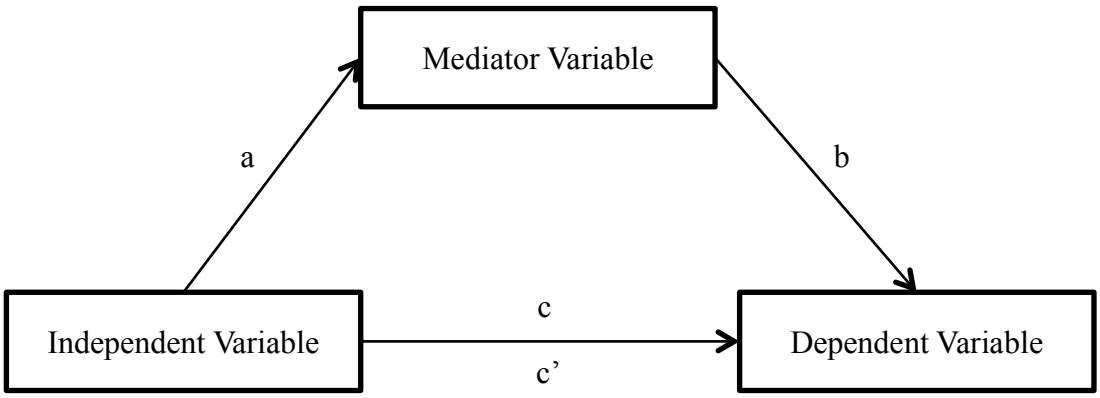

Figure 1. Mediation analysis model (Baron & Kenny, 1986).

Hypothesis 8

Higher rates of polypharmacy will yield a greater number of medications prescribed to address pharmacological side effects. The relationship between polypharmacy (independent variable) and number of medications prescribed to treat side effects resulting from polypharmacy (dependent variable) was examined using linear regression analysis.

CHAPTER 3

RESULTS

Demographics

Of the 182 participants, 80.8% were male (n = 147). The majority were Caucasian (55.5%; n = 101) or African American (40.1%; n = 73), with the remainder self-identified as Hispanic, Asian, Native American, or unknown/mixed race (4.3%; n = 8). The average age at time of admission to the facility was 32.5 years (SD = 11.6 years), with a mean age at discharge of 40.5 years (SD = 12.7 years).

Adverse Childhood Experiences

A majority of participants were exposed to childhood adversity (75.8%; n = 138), with an average ACE score of 2.63 (SD = 2.3). Of the total sample, 25.6% were exposed to four or more ACEs (n = 47). Total cumulative ACE scores are described in Table 1. Childhood abuse and neglect were prevalent within the sample, with reported rates as follows: physical abuse (35.7%; n = 65), sexual abuse (33.0%; n = 60), emotional abuse (24.2%; n = 44), and neglect (17.6%; n = 32). Nearly one-fifth of participants witnessed domestic violence toward a parent in their home (19.2%; n = 35). Over one-third of participants' parents were divorced or separated during their childhood (35.7%; n = 65), and 5.5% had a parent or guardian incarcerated (n = 10). Just over one-fourth of the sample reported one or both parents to have suffered with at least one mental illness (25.3%; n = 46), and 32.4% reported a parent with known substance abuse during their childhood (n = 59).

Table 1

ACE Score (N = 182)

ACE Score	*n* (%)
0	44 (24.2)
1	41 (22.5)
2	32 (17.6)
3	18 (9.9)
4	9 (4.9)
5	21 (11.5)
6	7 (3.8)
7	7 (3.8)
8	2 (1.1)
9	1 (0.5)
10	0 (0.0)

Clinical Functioning

As expected from participants' current admission to secure forensic inpatient care, psychiatric diagnoses were common. Descriptions of DSM-IV-TR (American Psychological Association, 2000) diagnostic categories are listed in Table 2. Participants were diagnosed with an average of 3.37 mental health symptom categories (*SD* = 1.65). Axis I disorders were diagnosed in 98.9% (*n* = 180) of the total sample. Psychotic and mood disorders were the most common Axis I disorders. Additional variables describing psychiatric functioning were examined. Of the total participants, 41.8% had a reported history of at least one suicide attempt (*n* = 76). Approximately 46% of participants had a history of self-injurious behavior (*n* = 83). A majority of participants exhibited a history of institutional aggression (86.8%; *n* = 158). Average length of admission was 8.01 years (*SD* = 7.11), with an average of 14.78 (*SD* = 12.27) separate instances of psychiatric admission.

Table 2

Frequency of Psychiatric Disorders (N=182)

Psychiatric Disorder	n (%)
Mood Disorders	83 (45.6)
Anxiety Disorders	16 (8.8)
Post-Traumatic Stress Disorder	24 (13.2)
Psychotic Disorders	109 (59.9)
Attention Deficit Hyperactivity Disorder	18 (9.9)
Impulse Disorders	41 (22.5)
Intellectual Disability / Cognitive / Developmental Disorders	105 (57.7)
Sexual Disorders	12 (6.6)
Anti-Social Personality Disorder	14 (7.7)
Borderline Personality Disorder	11 (6.0)
Other Psychiatric Disorders	35 (19.2)

Prescription Practices

Within the total sample of 182 participants, 131 participants' were prescribed psychotropic medications. Of these 131 participants, nearly all were prescribed at least two psychotropic medications (n = 129; 98.5%) with a mean number of psychotropic medications of 5.23 (SD = 2.20) and a range of zero to thirteen total different psychotropic medications prescribed to a given individual. Frequencies of psychotropic medication prescription, by number of medications, are provided in Table 3. A majority of patients were prescribed at least four different categories of psychotropic medications (n = 100; 75.7%) with a mean of approximately four different categories of psychotropic medications being prescribed to patients (M = 3.99, SD = 1.12). Significantly more individuals were prescribed four or more prescriptions than not (t = 27.162, p < 0.001). The most common types of medications include those with an on-label use of addressing mood (n = 121; 92.4%), psychotic (n = 117; 89.3%) and anxiety (n = 112; 85.5%) symptom concerns. Patients were prescribed an average of 2.30 (SD =

1.29) mood stabilizers, 2.17 (*SD* = 1.73) anxiolytics, and 1.71 (*SD* = 0.98) antipsychotic medications.

Table 3

Frequency of Number of Psychotropic Medications

Number of Psychotropic Medications	*n* (%)
0	2 (1.1)
1	0 (0.0)
2	11 (8.4)
3	11 (8.4)
4	28 (21.4)
5	26 (19.8)
6	19 (14.5)
7	17 (13.0)
8	10 (7.6)
9	1 (0.8)
10 or more	6 (4.7)

Clinical Functioning and Prescription Practices

Hypothesis 1

Patients with more mental health diagnoses will exhibit a greater degree of psychotropic polypharmacy. Poisson and logistic regression analyses were used to assess the relationship between number of mental health diagnostic categories and prescription practices. All analyses controlled for age, gender, and race. Gender (male and female) and race (white and non-white) were coded as dummy variables.

To examine the relationship between mental health and psychotropic prescription practices, the relationship between total number of mental health diagnostic categories and prescription practices of the total sample of 182 participants was evaluated. A significant Poisson regression model predicting psychotropic prescription practices emerged, with higher mental health disorder diagnoses being predictive of higher numbers of prescription medications (Table

4). That is, for every additional mental health diagnostic category, 1.055 (95% CI [1.012 to 1.100]) psychotropic prescriptions were given ($p = 0.013$). More specifically, the model was significant for prescriptions of mood-stabilizing medications, indicating that regardless of a diagnosed mood disorder, with each mental health diagnosis an additional 1.098 (95% CI [0.873 to 1.445]) mood-stabilizers were prescribed ($p = 0.016$).

Logistic regression analysis produced a significant model describing the effects of mental health disorder diagnosis on psychotropic polypharmacy ($\chi^2 = 5.772$, Nagelkerke's $R^2 = 0.098$, $p = 0.016$). Specifically, increases in mental health disorder diagnoses were associated with increased likelihood of psychotropic polypharmacy ($OR = 1.407$; 95% CI [0.975, 1.798]; Table 4). Models examining the association between mental health disorder diagnosis and antipsychotic polypharmacy and mood-stabilizer polypharmacy were not significant.

Table 4

Mental Health Disorder Effect on Psychotropic Prescription Practices

	B	SE	Wald χ^2	*p*	Exp(B)
# Psychotropic Medications	.053	.021	6.227	.013	1.055
Psychotropic Polypharmacy	.342	.151	5.101	.024	1.407

Hypothesis 2

Patients with serious mental illness diagnoses will exhibit a greater degree of polypharmacy. Poisson and logistic regression analyses were used to examine the relationship of diagnosed serious mental illness and psychotropic prescription practices (Table 5). While a diagnosis of at least one serious mental illness was not predictive of increased numbers of psychotropic prescriptions nor psychotropic polypharmacy, results indicate a significant relationship with antipsychotic polypharmacy ($\chi^2 = 5.334$, Nagelkerke's $R^2 = 0.054$, $p = 0.021$). The model correctly classified 64.1% of cases. Participants diagnosed with a serious mental

illness were 2.747 times more likely to be subject to antipsychotic polypharmacy than those without a serious mental illness.

Table 5

Serious Mental Illness and Psychotropic Prescription Practices

	B	SE	Wald χ^2	*p*	Exp(B)
# Psychotropic Medications	.727	.790	.845	.358	2.068
Psychotropic Polypharmacy	-.705	.659	1.144	.285	.494

Hypothesis 3

Patients with longer length of hospitalization will evidence greater polypharmacy. Length of hospitalization was not significantly related to psychotropic polypharmacy prescription practices (Table 6).

Table 6

Correlational Relationships Between ACE Score Variables, Behavioral Markers, and Psychotropic Medication Practices

	Total ACE Score	4+ ACE Score	# Psychotropic Medications	Psychotropic Polypharmacy
Hx Self-harm	.386**	.262**	.218*	.280**
Hx Suicide Attempts	.141	.086	.095	.032
Hx Institutional Aggression	.119	.084	.284*	.241**
# Previous Psychiatric Admissions	.102	.207*	.192*	.133
Length of Admission	.115	.126	.106	.094

*p<.05, **p<.01, ***p<.001

Hypothesis 4

Regardless of diagnosis, higher ACEs will be predictive of greater polypharmacy use. A significant model relating total cumulative ACE score to number of mental health symptom categories and prescription practices emerged (Table 7). Total ACE score was predictive of total mental health diagnoses (1.078, 95% CI [1.042, 1.116], p<0.001). Total number of mental health

diagnostic categories was thus controlled for in further analyses. Poisson regression produced a model predictive of a higher number of psychotropic prescriptions, with an increase of one on the total ACE score yielding a predicted increase of medications by 1.075 (95% CI [1.007, 1.147], $p = 0.030$). An increase in total ACE score was associated with increased risk of psychotropic polypharmacy ($OR = 1.313$; $p=0.035$).

Table 7

Regression Analyses of Total ACE Score to Psychotropic Polypharmacy Practices

	B	SE	Wald χ^2	*p*	Exp(B)
# Psychotropic Medications	.072	.0331	4.729	.030	1.075
Psychotropic Polypharmacy	.273	.130	4.426	.035	1.313

An evaluation of the average number of psychotropic prescriptions per each increase in ACE score was completed (Figure 2). A graded relationship between ACE score and prescriptions was observed. Models examining the association between total ACE score, total number of types of psychotropic medications, total number mood stabilizers, and total number of antipsychotic medications were not significant.

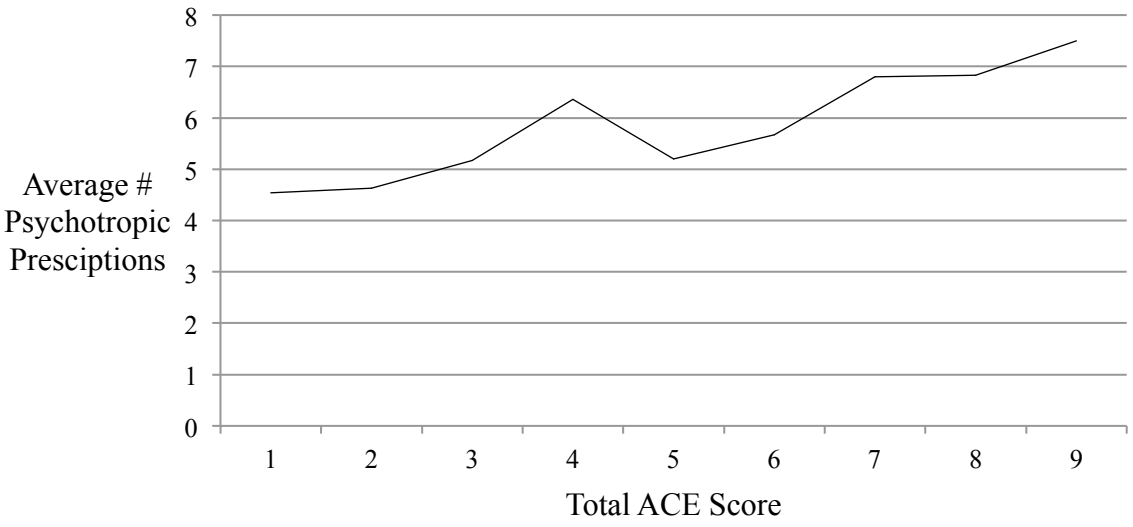

Figure 2. *Average Psychotropic Prescriptions per ACE Score*

Participants with an ACE score of four or higher were prescribed significantly more psychotropic medications ($F = 5.079$, $R^2 = 0.038$, $p = 0.026$). Interestingly, those with four or more ACEs were 5.123 ($p = 0.033$) times more likely to experience psychotropic polypharmacy than those with fewer than four ACEs ($\chi^2 = 6.498$, Nagelkerke's $R^2 = 0.079$, $p = 0.011$; Table 8). Additionally, participants with four or more ACEs were 3.362 ($p = 0.041$) times more likely to be prescribed an antipsychotic medication regardless of being diagnosed with a serious mental illness ($\chi^2 = 3.947$, Nagelkerke's $R^2 = 0.042$, $p = 0.047$).

Table 8

Regression Analyses of 4+ ACE Scores to Psychotropic Polypharmacy Practices

	B	SE	Wald χ^2	*p*	Exp(B)
# Psychotropic Medications	1.120	.253	4.271	.026	2.254
Psychotropic Polypharmacy	1.634	.767	4.535	.033	5.123

Hypothesis 5

Demographic factors, including age, gender, and race/ethnicity, will affect polypharmacy use. Linear regression analysis produced a significant model (Table 9) predicting earlier age of being prescribed a psychotropic medication as related to white ethnicity ($F = 4.658$, $R^2 = 0.115$, $p = 0.038$). White participants were prescribed their first psychotropic medication, on average, during adolescence ($M = 13.47$, $SD = 9.58$, range = 4-43), while non-white participants were prescribed their first psychotropic medication in adulthood ($M = 20.26$, $SD = 9.81$, range = 9-49).

Table 9

White Ethnicity Predictive of Earlier Age Prescribed Psychotropic Medications

	B	SE	β	*t*	*p*
Age	-6.789	3.146	-.338	-2.158	.038

Race was coded as white and non-white for comparison of nearly equal groups. Race was not significantly related to other prescription practices. No significant differences were found for gender and age related to prescription practices (Table 10).

Table 10

Correlations: Gender, Age, and Race Relationship to Psychotropic Prescription Practices

Variables	Total # Psychotropic Medications	Psychotropic Polypharmacy
Gender	-.093	-.056
Race	-.170	.005
Age	-.063	-.016

*p<.05, **p<.01, ***p<.001

Hypotheses 6 and 7

Patients with prior histories of self-harm, suicide attempts, institutional aggression, or lengthier occurrences of psychiatric hospitalization will be prescribed a greater number of psychotropic medications. Additionally, patients with prior histories of self-harm, suicide attempts, institutional aggression, or lengthier occurrences of psychiatric hospitalization will experience greater antipsychotic and mood-stabilizing polypharmacy. Poisson and logistic regression analyses were used to assess the relationship between behavioral factors and psychotropic medication prescription practices for the total sample of 182 participants. Behavioral factors include history of self-harm, history of suicide attempts, and history of institutional aggression. Total ACE score and an ACE score of four or more served as independent variables. Mediating variables included history of self-harm, history of suicide, history of aggression, and institutionalization history. Total number of psychotropic medications prescribed and psychotropic polypharmacy served as dependent variables.

History of self-harm. A significant Poisson regression model predicting psychotropic prescription practices emerged, with history of self-harm being predictive of higher numbers of psychotropic medications (Table 11). Persons with history of self-harm are expected to have 1.832 (95% CI [0.714, 0.910], p=0.018) times greater the number of psychotropic medications prescribed. Logistic regression analysis produced a significant model of the effects of history of self-harm on presence of psychotropic polypharmacy (χ^2 = 10.436, Nagelkerke's R^2 = 0.230, p = 0.001). Specifically, a history of self-harm was associated with a 5.060 increased likelihood of psychotropic polypharmacy (95% CI [3.957, 6.889], p=0.003).

Table 11

History of Self-Harm Predictive of Increased Psychotropic Medication Practices

	B	SE	Wald χ^2	*p*	Exp(B)
# Psychotropic Medications	.584	.278	5.605	.018	1.832
Psychotropic Polypharmacy	1.621	.546	8.831	.003	5.060

Logistic and Poisson regression analyses were used to investigate the effect of total ACE score, high ACE score, and history of self-harm on total psychotropic medications prescribed and psychotropic polypharmacy. Mediation analyses were conducted for those variables, as an initial significant relationship was found.

Results indicated that total ACE score was significantly predictive of total number of prescribed psychotropic medications (path c=.244, SE=.087, p=.006). Total ACE score was a significant predictor of a history of self-harm behaviors (path a =.409, SE = .086, p < .001). However, history of self-harm did not significantly predict the total number of psychotropic medications prescribed (path b=.650, SE=.408, p=.061) and, therefore, did not support a meditational relationship (Table 12).

Table 12

Mediation Analyses of ACE Score and Total Number Psychotropic Medications by History of Self-Harm

Regression paths	*B*	*SE*	*t*	*Wald*	*p*
Mediation *a* path (ACE Score on Hx Self-harm)	.409	.086	-	22.433	<.001
Mediation *b* path (Hx Self-harm on # Psy Medications)	.650	.408	1.591	-	.061
Total Effect *c* path (ACE Score on # Psy Medications)	.244	.087	2.809	-	.006
Direct Effect *c'* (ACE Score on # Psy Medications with Hx Self-harm mediator)	.186	.094	1.973	-	.114

No mediation (*b* path), therefore no indirect effect calculated.

Results indicated that having four or more ACEs was significantly predictive of total number of prescribed psychotropic medications (path c=.818, SE=.439, *p*=.045). An ACE score of four or greater was also a significant predictor of history of self-harm (path a =1.239, SE=.368, *p*=.001). Within this model, history of self-harm significantly predicted total number of psychotropic medications (path b=.831, SE=.394, *p*=.037). Finally, having four or more ACEs was no longer a significant predictor of total number of psychotropic medications when controlling for history of self-harm (path c'=.567, SE=.453, *p*=.213), consistent with full mediation (Figure 3).

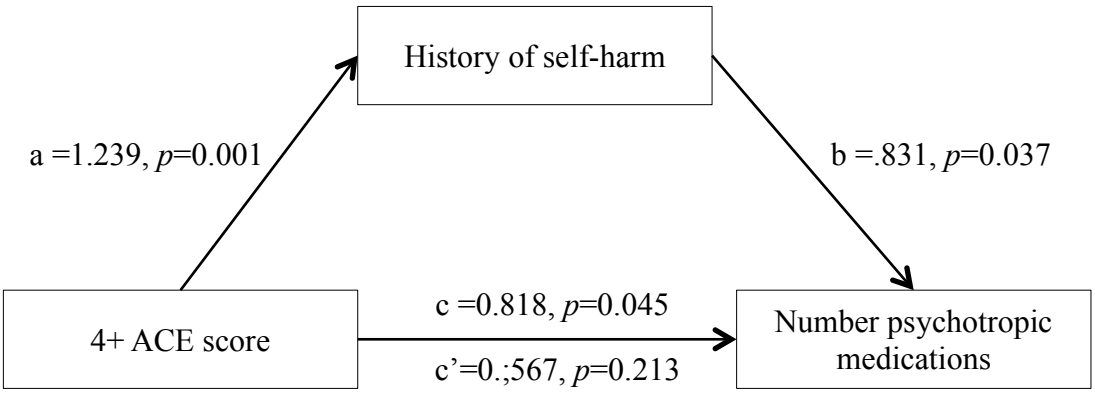

Figure 3. *Full Mediation of 4+ ACE Score and Total Number Psychotropic Medications by History of Self-Harm*

Approximately 33% of the variance in psychotropic prescriptions was accounted for by having four or more ACEs and history of self-harm (R^2=.326). The indirect effect was tested using a bootstrap estimation approach with 5000 samples (Adjei & Karim, 2016). These results indicated the indirect coefficient was significant (b=1.030, SE=.217, 95% CI [.432, 1.416]; Table 13).

Table 13

Mediation Analyses of 4+ ACE Score and Total Number Psychotropic Medications by History of Self-Harm

Regression paths	*B*	*SE*	*t*	*Wald*	*p*	*95% CI*
Mediation *a* path (4+ ACE Score on Hx Self-harm)	1.239	.368	-	11.342	.001	
Mediation *b* path (Hx Self-harm on # Psy Medications)	.831	.394	2.109	-	.037	
Total Effect *c* path (4+ ACE Score on # Psy Medications)	.818	.439	1.861	-	.045	
Direct Effect *c'* (4+ ACE Score on # Psy Medications with Hx Self-harm mediator)	.567	.453	1.252	-	.213	
Indirect Effect (c – c') bootstrapped [95% CI]	1.030	.217				[.432, 1.416]

Results indicated that total ACE score was significantly predictive of the presence of psychotropic polypharmacy (path c =.273, SE=.130, *p*=.035). As stated previously, total ACE score was a significant predictor of a history of self-harm behaviors (path a =.409, SE=.086, *p*<.001). A history of self-harm was a significant predictor of psychotropic polypharmacy (path b =1.469, SE=.581, *p*=.011). Total ACE score was no longer a significant predictor of psychotropic polypharmacy after controlling for history of self-harm (path c' = .097, SE=.137, *p*=.478), consistent with full mediation (Figure 4).

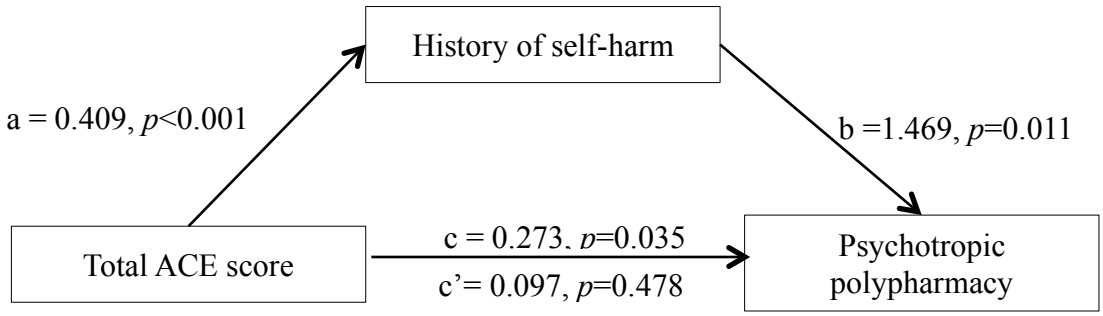

Figure 4. *Full Mediation of Total ACE Score and Psychotropic Polypharmacy Relationship by History of Self-Harm*

Approximately 52% of the variance in psychotropic polypharmacy was accounted for by total ACE score and history of self-harm (R^2 = .521). The indirect effect was tested using a bootstrap estimation approach with 5000 samples (Adjei & Karim, 2016).. These results indicated the indirect coefficient was significant (b =.601, SE=.061, 95% CI [.265, .926]; Table 14). Total ACE score was associated with a .60 increase in the likelihood of being prescribed four or more psychotropic medications, as mediated by history of self-harm.

Table 14

Mediation Analyses of Total ACE Score and Psychotropic Polypharmacy by History of Self-Harm

Regression paths	*B*	*SE*	*Wald*	*p*	*95% CI*
Mediation *a* path (ACE Score on Hx Self-harm)	.409	.086	22.433	<.001	
Mediation *b* path (Hx Self-harm on Psy Polypharmacy)	1.469	.581	6.403	.011	
Total Effect *c* path (ACE Score on Psy Polypharmacy)	.273	.130	4.426	.035	
Direct Effect *c'* (ACE Score on Psy Polypharmacy with Hx Self-harm mediator)	.776	.354	4.812	.028	
Indirect Effect (c – c') bootstrapped [95% CI]	.601	.061			[.265, .926]

An ACE score of four or higher was significantly predictive of psychotropic polypharmacy (path c =1.634, SE=.767, *p*=.033). Having four or more ACEs was a significant

predictor of a history of self-harm (path a =1.239, SE=.368, *p*=.001). History of self-harm behaviors was a significant predictor of psychotropic polypharmacy (path b =1.427, SE=.557, *p*=.010). An ACE score of four or higher was no longer significantly predictive of psychotropic polypharmacy after controlling for history of self-harm (path c'=1.164, SE=.792, *p*=.142), consistent with full mediation (Figure 5).

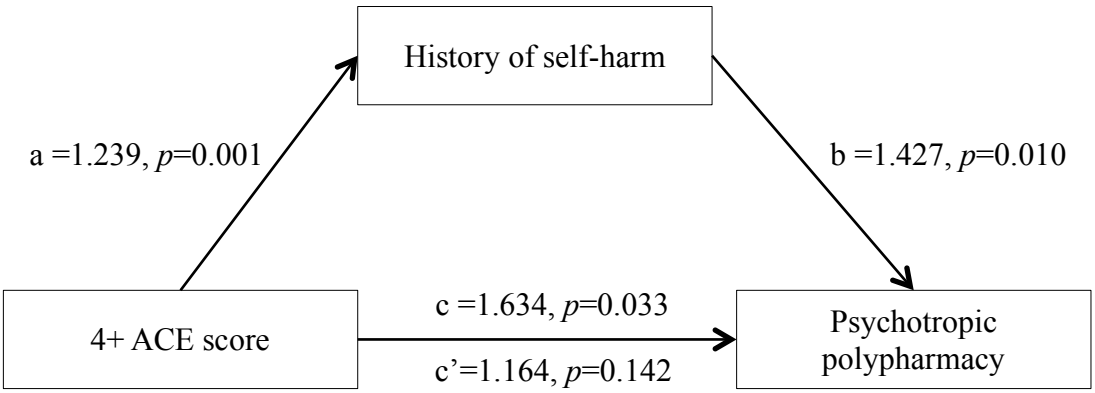

Figure 5. *Full Mediation of 4+ ACE Score and Psychotropic Polypharmacy by History of Self-Harm*

Approximately 19% of the variance in psychotropic polypharmacy was accounted for by an ACE score of four or greater and history of self-harm (R^2=.193). These results indicated the indirect coefficient was significant (b =1.768, SE=.471, 95% CI [1.026, 1.954]; Table 15).

Table 15

Mediation Analyses of 4+ ACE Score and Psychotropic Polypharmacy by History of Self-Harm

Regression paths	*B*	*SE*	*Wald*	*p*	*95% CI*
Mediation *a* path (4+ ACE Score on Hx Self-harm)	1.239	.368	11.342	.001	
Mediation *b* path (Hx Self-harm on Psy Polypharmacy)	1.427	.557	6.571	.010	
Total Effect *c* path (4+ ACE Score on Psy Polypharmacy)	1.634	.767	4.535	.033	
Direct Effect *c'* (4+ ACE Score on Psy Polypharmacy with Hx Self-harm mediator)	1.164	.792	2.156	.142	
Indirect Effect (c – c') bootstrapped [95% CI]	1.768	.471			[1.026, 1.954]

History of suicide. No significant relationship was found when examining the association between history of previous suicide attempts, and psychotropic prescription practices was not significant (see Table 4).

History of institutional aggression. A significant model relating history of aggression and psychotropic prescription practices emerged (Table 16). History of aggression was predictive of total number of psychotropic medications (0.570, 95% CI [0.397, 0.817], $p = 0.002$). Logistic regression results also indicated a significant relationship between history of aggression and presence of psychotropic polypharmacy ($\chi^2 = 5.767$, Nagelkerke's $R^2 = 0.073$, $p = 0.016$). Participants with a history of aggression were 5.444 (p=0.013) times more likely to experience psychotropic polypharmacy than those without a history of aggression.

Table 16

Aggression Relationship to Psychotropic Medication Practices

	B	SE	Wald χ^2	*p*	Exp(B)
# Psychotropic Medications	.562	.184	9.343	.002	.570
Psychotropic Polypharmacy	1.695	.682	6.166	.013	5.444

More specifically, Poisson regression produced a model predictive of a higher number of mood stabilizing and antipsychotic medications for persons with a history of aggression. Persons with history of aggression are expected to have a mood stabilizer/antipsychotic medication rate 1.488 (95% CI [1.286, 1.832], $p = 0.008$) times greater than those without history of aggression. Logistic regression analysis produced a significant model of the effects of history of aggression on mood stabilizer polypharmacy ($\chi^2 = 6.226$, Nagelkerke's $R^2 = 0.082$, $p = 0.013$). Specifically, participants with a history of aggression were 5.460 (p=0.013) times more likely to be subject to mood stabilizer polypharmacy than those without a history of aggression.

Results indicated that total ACE score was significantly predictive of total number of prescribed psychotropic medications (path c=.244, SE=.087, *p*=.006). However, total ACE score did not significantly predict of a history of aggression (path a =.246, SE= .162, *p*=.129). Therefore, a meditational relationship of total ACE score and psychotropic medication practices by history of aggression was not statistically supported (Table 17).

Table 17

Mediation Analyses of Total ACE Score and Psychotropic Medication Practices by History of Institutional Aggression

Regression paths	*B*	*SE*	*t*	*Wald*	*p*
Mediation *a* path (ACE Score on Hx Institutional Aggression)[1]	.246	.162	-	2.300	.129
Mediation *b* path (Hx Institutional Aggression on # Psy Medications)	2.084	.683	3.052	-	.003
Total Effect *c* path (ACE Score on # Psy Medications)	.212	.086	2.463	-	.015
Direct Effect *c'* (ACE Score on # Psy Medications with Hx Institutional Aggression mediator)	.244	.087	2.809	-	.006
Mediation *a* path (ACE Score on Hx Institutional Aggression)	.246	.162	-	2.300	.129
Mediation *b* path (Hx Institutional Aggression on Psy Polypharmacy)	1.505	.694	-	4.705	.030
Total Effect *c* path (ACE Score on Psy Polypharmacy)	.273	.130	-	4.426	.035
Direct Effect *c'* (ACE Score on Psy Polypharmacy with Hx Institutional Aggression mediator)	.238	.133	-	2.197	.074

No mediation (*a* path), therefore no indirect effect calculated.

Similarly, an ACE score of four or higher was significantly predictive of total number of psychotropic medications (path c=.818, SE=.268, *p*=.045). Having four or more ACEs was not significantly predictive of a history of aggression (path a =.840, SE= .784, *p*=.284); therefore, a mediation relationship between ACE score of four or greater and psychotropic medications with history of aggression was not supported (Table 18).

Table 18

Mediation Analyses of 4+ ACE Score and Psychotropic Medication Practices by History of Institutional Aggression

Regression paths	*B*	*SE*	*t*	*Wald*	*p*
Mediation *a* path (4+ ACE Score on Hx Institutional Aggression)	.840	.784	-	1.147	.284
Mediation *b* path (Hx Institutional Aggression on # Psy Medications)	2.190	.690	3.175	-	.002

Regression paths	*B*	*SE*	*t*	*Wald*	*p*
Total Effect *c* path (4+ ACE Score on # Psy Medications)	.818	.439	1.861	-	.065
Direct Effect *c'* (4+ ACE Score on # Psy Medications with Hx Institutional Aggression mediator)	.702	.434	1.618	-	.108
Mediation *a* path (4+ ACE Score on Hx Institutional Aggression)	.840	.784	-	1.147	.284
Mediation *b* path (Hx Institutional Aggression on Psy Polypharmacy)	1.520	.697	-	4.752	.029
Total Effect *c* path (4+ ACE Score on Psy Polypharmacy)	1.634	.767	-	4.535	.033
Direct Effect *c'* (4+ ACE Score on Psy Polypharmacy with Hx Institutional Aggression mediator)	1.528	.777	-	3.870	.049

No mediation *(a* path), therefore no indirect effect calculated.

History of psychiatric hospitalizations. A lengthier history of psychiatric hospitalizations, as measured by number of previous admissions, was predictive of several varied psychotropic medication prescription practices. A significant Poisson regression model predicting psychotropic prescription practices emerged (Table 19), with lengthier history of psychiatric hospitalizations being predictive of higher numbers of psychotropic medications. For every additional hospitalization, a 1.007 (95% CI [1.000, 1.014], p = 0.038) increase in the number psychotropic medications, and, more specifically, a 1.012 (95% CI [1.002, 1.022], *p* = 0.017) increase in the number of mood-stabilization medications, was observed.

Table 19

Lengthier History of Psychiatric Hospitalization Predicive of Psychotropic Prescription Practices

	B	SE	Wald χ^2	*p*	Exp(B)
# Psychotropic Medications	.007	.004	4.289	.038	1.007
Psychotropic Polypharmacy	.268	.074	5.349	.017	1.012

Total ACE score was significantly predictive of total number of psychotropic medications (path c=.244, SE=.087, *p*=.006) and psychotropic polypharmacy (path c =.273, SE=.130, *p*=.035). No significantly predictive relationship was found for total ACE score and lengthier institutionalization history; therefore, no meditational relationship was supported (Table 20).

Table 20

Mediation Analyses of Total ACE Score and Psychotropic Medication Practices by Number of Psychiatric Admissions

Regression paths	*B*	*SE*	*t*	*Wald*	*p*
Mediation *a* path (ACE Score on # Psychiatric Hospitalization)	.870	.493	2.026	-	.045
Mediation *b* path (# Psychiatric Hospitalization on # Psy Medications)	.032	.019	1.709	-	.090
Total Effect *c* path (ACE Score on # Psy Medications)	.244	.087	2.809	-	.006
Direct Effect *c'* (ACE Score on # Psy Medications with # Psychiatric Hospitalization mediator)	.220	.090	2.437	-	.016
Mediation *a* path (ACE Score on # Psychiatric Hospitalization)	.576	.431	1.335	-	.184
Mediation *b* path (# Psychiatric Hospitalization on Psy Polypharmacy)	.030	.027	-	1.246	.264
Total Effect *c* path (ACE Score on Psy Polypharmacy)	.273	.130	-	4.426	.035
Direct Effect *c'* (ACE Score on Psy Polypharmacy with # Psychiatric Hospitalization mediator)	.248	.132	-	3.534	.060

Having four or more ACEs was significantly associated with total number of psychotropic medications (path c =818, SE=.439, *p*=.033) and psychotropic polypharmacy (path c =1.634, SE=.767, *p*=.065); however, no significant relationship was found between an ACE score of four or higher and lengthier history of institutionalization (path a =3.229, SE=2.145, *p*=.134; Table 21).

Table 21

Mediation Analyses of 4+ ACE Score and Psychotropic Medication Practices by Number of Psychiatric Admissions

Regression paths	*B*	*SE*	*t*	*Wald*	*p*
Mediation *a* path (4+ ACE Score on # Psychiatric Hospitalization)	5.147	2.138	2.408	-	.018
Mediation *b* path (# Psychiatric Hospitalization on # Psy Medications)	.035	.019	1.802	-	.074
Total Effect *c* path (4+ ACE Score on # Psy Medications)	.818	.439	1.861	-	.065
Direct Effect *c'* (4+ ACE Score on # Psy Medications with # Psychiatric Hospitalization mediator)	.650	.463	1.405	-	.163
Mediation *a* path (4+ ACE Score on # Psychiatric Hospitalization)	3.229	2.145	1.506	-	.134
Mediation *b* path (# Psychiatric Hospitalization on Psy Polypharmacy)	.026	.026	-	.979	.322
Total Effect *c* path (4+ ACE Score on Psy Polypharmacy)	1.634	.767	-	4.535	.033
Direct Effect *c'* (4+ ACE Score on Psy Polypharmacy with # Psychiatric Hospitalization mediator)	1.498	.782	-	3.671	.055

Hypothesis 8

Higher rates of polypharmacy will yield a greater number of medications prescribed to address pharmacological side effects. A linear regression was calculated to predict the number of medications prescribed to aid with pharmacological side effects based on total number of

medications prescribed (Table 22). A significant equation was found ($F(1, 129)=8.457$, $p=0.004$), with an R^2 of 0.248.

Table 22

Number of Medications Prescribed Effect on Medications Prescribed to Address Pharmacological Side Effects

	B	SE	β	*t*	*p*
# Side Effect Medications	.048	.016	.248	2.908	.004

Additionally, linear regression analysis (Table 23) indicated that the total number of different psychotropic medications was predictive of number of medications prescribed to aid with pharmacological side effects, with 32.9% of the variance explained ($F(1, 129)=15.651$, $p<0.001$).

Table 23

Number of Different Types of Psychotropic Medications Prescribed Effect on Medications Prescribed to Address Pharmacological Side Effects

	B	SE	β	*t*	*p*
# Side Effect Medications	.126	.032	.329	3.956	<.001

Unexpectedly, a significant inverse relationship was found showing the more mood stabilizers, anxiolytics, and or antipsychotics prescribed, the fewer number of medications were prescribed to address pharmacological side effects ($F(1, 129)=4.444$, $p=.037$), with an R^2 of 0.033. Participants' side effect medications decreased 0.243 for each mood stabilizer, anxiolytic, or antipsychotic medication.

CHAPTER 4

DISCUSSION

Little research has examined the relationship between ACEs, related negative outcomes, and psychotropic prescription practices. No research to date has examined these relationships within forensic mental health populations, who experience markedly increased ACEs, psychopathology, and polypharmacy. This study evaluated the presence of ACEs and their impact on prescription practices, as well as the relationship between ACEs, prescription practices, and specific behavioral markers of mental and emotional health.

Participants in the current sample evidenced rates of ACEs that exceed those reported in community samples, with one-fourth having experienced four or more childhood adversities. The more childhood adversity and dysfunction experienced, the poorer the mental health outcomes, with total ACE score predicting an increased number of mental health diagnostic categories. Participants were diagnosed, on average, with three to four distinct mental health diagnostic symptom categories. Furthermore, nearly half of the participants were diagnosed with a mood disorder and three-fifths with a psychotic disorder.

As expected, the more mental health disorder categories a participant was diagnosed with, the more psychotropic medications were prescribed and the greater the risk of psychotropic polypharmacy. Participants were prescribed approximately five psychotropic medications in total, and, on average, approximately four different types of psychotropic medications. For those diagnosed with at least one serious mental illness (SMI), the risk of being prescribed two or more antipsychotic medications was nearly three-fold.

Regardless of number of mental health diagnoses, a graded relationship was established between ACE score and prescribed psychotropic medications. As number of ACEs increased, the

risk of psychotropic polypharmacy increased as well. For those who endorsed higher-end ACE scores, there was a five times greater risk of experiencing psychotropic polypharmacy compared to those with fewer than four ACEs. More specifically, those with four or more ACEs were over three times as likely to be prescribed antipsychotic medications regardless of an SMI diagnosis.

Demographic Factors

Other factors and their relationship to prescription practices and ACE score were explored. In relation to demographic factors, white participants were prescribed psychotropic medications far earlier in life. In fact, on average, white participants received their first psychotropic prescription in adolescence as compared to non-white participants who were not, on average, prescribed a psychotropic medication until early adulthood. There are several potential explanations. Within minority populations, some studies have suggested higher prevalence of psychiatric disorders (Pumariega, Rogers, & Rothe, 2005); however, many minority youth who display disruptive or aggressive behaviors are referred to the juvenile justice system without consideration of the possibility that they may be experiencing untreated mental health problems (Bronsard et al., 2017; Garland, Hough, McCabe, Yeh, Wood, & Aaron, 2001). Furthermore, significant diagnostic disparities have been found within samples of minority youths. Some evidence suggests question phrasing may lead to response bias in minority populations (Alegria, Vallas, & Pumariega, 2010). These behavioral and diagnostic assumptions may lead to lower estimations of mental health needs, thus delaying pharmacologic intervention.

Should a person require psychotropic medications related to specific diagnosed mental health conditions, the discrepancy in prescription practices by race may additionally be explained by the general disparities in access to healthcare and treatment for mental illness. These disparities have persisted, with fewer racial minorities having health insurance and fewer

receiving mental health treatment (U.S. Department of Health & Human Services, 2015). Additionally, racial minorities hold more conservative beliefs concerning mental illness and receiving related services. Ward and colleagues (2013) found that black or African American individuals perceived greater stigma related to psychological diagnoses and help-seeking behaviors, which led to participants more limitedly acknowledging psychological problems and being minimally open to seeking mental health services. The health care disparities and cultural stigma may further explain why white participants received their first psychotropic medication at a much younger age than non-white participants.

Length and Prior History of Hospitalization

Higher incidents of prior hospitalization increased the likelihood of higher rates of psychotropic medications. More specifically, for each additional hospitalization, the likelihood of being prescribed two or more mood stabilizers increased. Unexpectedly, patients with longer hospitalizations did not showcase different trends in psychotropic prescription practices in comparison with those with shorter current hospitalization. Previous studies have identified associations between specific types of polypharmacy practices (e.g., antipsychotic polypharmacy) and lengthier hospitalizations (e.g., Suokas et al., 2012); however, these findings may be more representative of factors that would yield lengthier hospitalizations, like severity of psychological symptoms and related behavioral consequences. Additionally, patients receiving more concerning antipsychotic polypharmacy regimens are often admitted with this regimen, or it is initiated within the first six months of hospitalization (Lacasse, 2014), suggesting length of hospitalization is not a causal factor of psychotropic polypharmacy. It may be more appropriate to consider length of hospitalization as a marker for more severe and chronic illness, rather than as a risk factor for psychotropic polypharmacy.

With each increasing number of independent psychiatric hospitalizations, there may be an opportunity at each admission intake for re-evaluation and review of recent mental health and behavioral history to determine current medication need. This re-evaluation may yield a change in perception of need by providers because of the renewed ability to consider previously unaccounted for history and determine the change or persistence in current symptom presentation. Lacasse (2014) concluded that being previously committed to a psychiatric facility may elicit a stronger perception of risk and dangerousness, thus, influencing prescription practices.

While ACE score was not predictive of the number of prior hospitalizations when demographic factors and number of mental health diagnostic categories were taken into account, lengthier history of prior hospitalizations may represent persistence of mental illness and behavioral concerns. A more detailed examination of the reasons for various past hospitalizations may more effectively allow for an understanding of the relationship of ACE score and prescription practices in the context of previous hospitalizations.

Behavioral Markers

Several behavioral factors that may evidence more severe and chronic emotional and mental health concerns were explored. These behavioral markers must be considered within the context of the type of data collected (i.e., prescription count data). First line psychotropic medication treatment guidelines suggest giving an individual drug an adequate trial at therapeutic levels and within specific dosage recommendations to determine efficacy before considering polypharmacy (Moller et al., 2014). The data collected for this study did not allow for analysis of dosing. As such, behavioral histories of self-harm, suicide attempts, and institutional aggression

may have been addressed by adjusting the dosage of current prescriptions rather than adding additional psychotropic medications.

History of Self-Harm

A history of self-harm was associated with higher rates of psychotropic medications, with a risk of nearly five times greater for psychotropic polypharmacy regardless of types of mental health diagnoses. Taken together, experiencing childhood adversity and familial dysfunction leads to an increased number of psychotropic medications and psychotropic polypharmacy for self-harm behaviors. Abuse and neglect in childhood can contribute to difficulty regulating emotional responses and result in the employment of maladaptive emotional regulation behaviors (e.g., self-harm; Cleare et al., 2018). These behaviors are most likely expressions of symptomatic fluctuation and often in the context of emotional dysregulation and impulsivity. As a result, psychotropic polypharmacy may be a common outcome in an attempt to provide symptomatic relief (Madan et al., 2015).

History of Suicide Attempts

Suicide attempt history did not reveal varied prescription practices. While persons with suicidal behaviors may evidence more severe psychopathology, there is limited evidence that psychotropic medication management reduces long-term suicide risk (Baldesarini & Tondo, 2012). As a result, history of suicide attempts may have lesser impact on medication management than the acute nature of active suicidal ideation or behaviors.

History of Institutional Aggression

History of institutional aggression was predictive of higher numbers of psychotropic medications, as those with a history of aggression were 5.5 times more likely to experience psychotropic polypharmacy. Regardless of being diagnosed with a mood disorder or SMI,

participants with a history of institutional aggression were 1.5 times more likely to be prescribed multiple mood stabilizers and antipsychotics. These patients were five times more likely to be subject to mood stabilizer polypharmacy. This is consistent with and extends prior research in similar samples, in that patients in forensic inpatient settings are often prescribed at least one antipsychotic or mood stabilizer, often at higher dosing, to manage actual or perceived violent behavior (Deb et al., 2015; Krakowski, 2008; Lacassee, 2014; Swanson et al., 2008).

Cumulative ACE score was not predictive of history of institutional aggression. This may be a result of a ceiling effect, as over 92% of individuals had history of institutional aggression. This saturation in the sample, without further detail, may have prevented distinguishing a more specific relationship between ACE score and institutional aggression. Previous research has identified a positive link between experiences of abuse, neglect and household dysfunction during childhood and likelihood of perpetrating later violence (e.g., Duke et al., 2010; Reavis et al., 2013; Whitfield et al., 2003). However, definitive causal models have not been established in available research. Additionally, much of the research examining aggression and ACEs focuses on aggressive acts outside of the institutional environment and, if more specific, by behavioral categories of aggression (Goedhard, Stoller, Nijman, Egberts, & Heerdink, 2007) or aggression type (Dudeck et al., 2016). Research indicates different predictors for community versus institutional aggression (e.g., Young, Misch, Collins, & Gudjonsson, 2011). Further examination of ACEs, aggression, and other related factors is required to fully understand these relationships.

Psychotropic Polypharmacy Side Effect Management

Psychotropic polypharmacy was not unexpected, particularly in the context of multimorbidity common in forensic inpatient populations (Gnijdic et al., 2017). With most participants being diagnosed with multiple mental health disorders, it could be argued that a

regimen of one medication for each disorder is strictly rational. Nevertheless, this approach can lead to an increased side effect burden and problematic pharmacological interactions. This is especially true considering medication regimens that include treatment of medical diagnoses. For the current study's participants, the more medications prescribed, the higher the need for medications to address medication side effects. Particularly, higher rates of psychotropic medications had an equivocal need for increased prescriptions of medications to address related and often serious side effects.

Unexpectedly, an increase in mood stabilizing, anxiolytic, and/or antipsychotic medications resulted in a slight reduction in prescriptions to address medication side effects. Research suggests an increased need for medications to address extrapyramidal side effects with increased dosage and number of antipsychotics taken, as well as lengthier time taking these medications (Armstrong & Temmingh, 2017; Carnahan et al., 2006). While anticholinergic agents are commonly used medications for extrapyramidal side effects (Pringsheim et al., 2011), there is an increased risk of compounded side effects if these are combined with atypical antipsychotics (Campbell et al., 2009; Lieberman, 2004). Less commonly, dopamine agonist agents are also used to treat extrapyramidal side effects (Pringsheim et al., 2011). Dopamine receptor agonists have efficacy as an adjunctive intervention for treatment-resistant depression and mood disorders (Hori & Kunugi, 2012; Romeo, Blecha, Locatelli, Benyamina, & Martelli, 2018). Additionally, anxiolytics have been found to partially mimic dopamine agonists (Bartoszyk, 1998). Taken together, it may be that the addition of an anxiolytic helped manage extrapyramidal side effects, or that in the treatment of mood concerns a dopamine agonist or partial agonist was added to the medication regimen and, thus, aided in the management of

extrapyramidal side effects without the need to add a specific medication only to address these side effects.

Future Directions

The current findings provide valuable insight into the relationships between ACEs, psychopathology symptomology, and psychotropic prescription practices for persons within a secure forensic inpatient setting. This sample of individuals represents a unique and understudied group within the context of ACEs research and psychotropic polypharmacy.

ACE score indicates the presence of a limited set of adversities in childhood. It is not an all-encompassing indicator of childhood experience, however. In populations with high incidences of ACEs, there are other potential predictors that may emerge that more completely and precisely explain the impact of childhood adversity and household dysfunction on mental health outcomes, symptoms of mental illness, institutional aggression, and related prescription practices. Accordingly, future research should consider other components of adversity, including duration and severity of maltreatment, community adversity correlates (e.g., persistent violence within community), and specific ACE item relationship to identified outcomes. To more fully understand the role of early trauma and dysfunction, exploring the relationship of individual ACE items to demographic factors, mental health outcomes, and related prescription practices is a needed next step.

Also, examining prescription practices could be expanded beyond their on-label uses for diagnosed mental illnesses. The current study categorized prescriptions based on their on-label approved treatments. Future studies may more precisely distinguish rates and relationships to psychotropic polypharmacy by investigating the intended purpose of the medication (e.g., SSRI prescribed for sleep concerns rather than antidepressant). Additionally, having access to

medication dosing would provide a more complete picture of prescription practices. This is specifically concerning for those exhibiting self-harm, suicidality, and aggressive behaviors. While additional prescriptions may be the response to such behaviors, increasing the dosage of current medications may be the first line medication management response. This increase in dosage would not evidence increased polypharmacy practices, but may still carry with it negative side effects. As such, it is important to understand the complete picture of prescription practices for the most effective treatment approaches to be developed and understood.

To better understand the relationship of length of hospitalization and prescription practices, future research should account for drug regimens at admission, alterations made after initial assessment, and alterations throughout admission until discharge. Understanding the timeline of prescriptions, particularly at admission and discharge, could allow for a more detailed model encompassing risk of polypharmacy in relation to characteristics of hospitalization. Furthermore, ascertaining the reason for previous hospitalizations may evidence insight into the impact of chronic emotional and mental health outcomes on prescription practices. This may lead to a more in-depth evaluation of diagnosis and symptomology and related prescription practices (e.g., schizoaffective disorder versus schizophrenia; those with SMI that do and do not suffer with hallucinations). Taking into account the pervasiveness of certain symptomologies, historical versus current/acute symptoms, and the functional context of behaviors in the context of ACEs and prescription practices will allow for a more in depth perspective on these relationships, informing future prevention and intervention methods.

Limitations

There are a number of limitations of the current research. The sample was drawn from only one facility, which may limit generalizability. While the sample is smaller in size (*N*=182),

this is representative of the small nature of forensic mental health populations and is consistent with other empirical research focusing on this group. Despite the small sample, my findings are still informative for those working with these understudied groups. Additionally, this study was comprised of retrospective, archival data, which may be subject to recording error and does not allow for varied exploration of specific data points. However, the inclusion and exclusion criteria allow for a selection of records with detailed reports corroborated by participants' family members and official agencies.

Prescription count data allowed for several key analyses, but a more detailed examination of relationships would have been possible with additional information (e.g., medication dosing, length of time taking specific medications). A strength of the current study is that the data used are prescription data within a setting that has controlled medication distribution. This type of data reflects provider prescription practices and a stricter monitoring of prescribed medication adherence. As such, these data may be a more accurate portrayal of medications and adherence than self-report data.

The manner of recording data may also limit findings of the current study. Dichotomous recording of behavioral histories, though able to more conservatively estimate such a factor, provided limited information related to characteristics of aggression like pervasiveness, historical versus current, frequency, and severity. Future studies should seek to examine relationships between ACEs, behavioral histories, and prescription practices in less restricted ways.

Conclusion

Nuanced findings addressing the study aims allowed for filling gaps and extending current literature. The patterns and impact of polypharmacy were established and the relationship between prescription practices, ACEs, and related behavioral markers were examined.

The stark intricacy and sheer rates of psychotropic prescriptions and polypharmacy are concerning for the treatment and eventual outcomes of these patients, as prior research suggests increased likelihood of adverse drug events, concerning side effects, and decreased life expectancy associated with polypharmacy and psychotropic polypharmacy practices. Diagnostic accuracy and clarification may aid in assessing treatment needs. Even with complex needs, prescribers must review pharmaceutical regimens regularly, and when contemplating the addition of a psychotropic medication, must verify that superfluous medications are discontinued and interactions can be accounted for on an individual basis.

ACEs are a relevant consideration in the treatment of mental illness. Childhood adversity may lead to a lifetime of difficulty with managing emotional distress and symptoms of psychopathology. Pharmacological treatment may be necessary, particularly with populations who experience more complex mental health outcomes. However, a primary focus on psychotropic intervention can result in high rates of medications and polypharmacy with significant side effects. Individuals who have experienced higher incidents of childhood adversity may require unique treatment approaches, given additional associations between ACEs, aggression, self-harm, suicidality, and other factors associated with increased perceived behavioral and mental health symptoms that may prompt polypharmacy considerations. Additional treatment responses and incorporation of non-pharmacological intervention to circumvent the potential for psychotropic polypharmacy and related negative consequences is a crucial goal for these patients. Treatments that focus on addressing learned maladaptive coping strategies as well as addressing the current problem behaviors with an eye to addressing functional need are warranted. This may allow for lessened dependence on psychotropic

medications as a means of managing the complex nature of emotional and mental health needs commonly exhibited in forensic inpatient populations.

REFERENCES

Adjei, I.A. & Karim, R. (2016). An application of bootstrapping in logistic regression model. *Open Access Library Journal, 3* (e3049). doi: 10.4236/oalib.1103049

Afifi, T. O., Mather, A., Boman, J., Fleisher, W., Enns, M. W., MacMillan, H., & Sareen, J. (2011). Childhood adversity and personality disorders: Results from a nationally representative population-based study. *Journal of Psychiatric Research, 45*, 814-822. doi: 10.1016/j.jpsychires.2010.11.008

Allem, J., Soto, D. W., Baezconde-Garbanati, L., & Unger, J. B. (2015). Adverse childhood experiences and substance use among Hispanic emerging adults in Southern California. *Addictive Behaviors, 50*, 199-204.

Alpert, P. T. (2015). Issues surrounding polypharmacy. *Home Health Care Management & Practice, 27*(4), 256-258. doi: 10.1177/1084822314554281

Anda, R. F., Brown, D. W., Dube, S. R., Bremner, J. D., Felitti, V. J., & Giles, W. H. (2008). Adverse childhood experiences and chronic obstructive pulmonary disease in adults. *American Journal of Preventive Medicine, 34*(5), 396-403. doi: 10.1016/j.amepre.2008.02.002

Anda, R. F., Brown, D. W., Felitti, V. J., Bremner, J. D., Dube, S. R., & Giles, W. H. (2007). Adverse childhood experiences and prescribed psychotropic medications in adults. *American Journal of Preventative Medicine, 32*(5), 389-394. doi: 10/1016/j.amepre.2007.01.005

Anda, R. F., Croft, J. B., Felitti, V. J., Nordenberg, D., Giles, W. H., Williamson, D. F., & Giovino, G. A. (1999). Adverse childhood experiences and smoking during adolescence

and adulthood. *Journal of the American Medical Association, 282*(17), 1652-1658. doi: 10.1001/jama.282.17.1652

Anda, R., Tietjen, G., Schulman, E., Felitti, V., & Croft, J. (2010). Adverse childhood experiences and frequent headaches in adults. *Headache: The Journal of Head and Face Pain, 50*(9), 1473-1481. doi: 10.1111/j.1526-4610.2010.01756.x.

Armstrong, K. S. & Temmingh, H. (2017). Prevalence of and factors associated with antipsychotic polypharmacy in patients with serious mental illness: Findings from a cross-sectional study in an upper-middle-income country. *Revista Brasileira de Psiquiatria, 0*, 1-9. doi: 10.1590/1516-4446-2016-2015

Baglivio, M., Epps, N., Swartz, K., Sayedul Huq, M., Sheer, A., & Hardt, N. (2014). The prevalence of Adverse Childhood Experiences (ACE) in the lives of juvenile offenders. *Journal of Juvenile Justice, 3*(2), 1-23.

Baglivio, M. T., Wolff, K. T., Piquero, A. R., & Epps, N. (2015). The relationships between Adverse Childhood Experiences (ACE) and juvenile offending trajectories in a juvenile offender sample. *Journal of Criminal Justice, 43*, 229-241.

Barnes, T. R. E. & Paton, C. (2011). Antipsychotic polypharmacy in schizophrenia: Benefits and risks. *CNS Drugs, 25*(5), 383-399.

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic and statistical considerations. *Journal of Personality and Social Psychology, 51*, 1173-1182.

Beck, N. C., Hammer, J. H., Robbins, S., Tubbesing, T., Menditto, A., & Pardee, A. (2017). Highly aggressive women in a forensic psychiatric hospital. *The Journal of the American Academy of Psychiatry and the Law, 45*(1), 17-24.

Bellis, M. A., Hughes, K., Leckenby, N., Jones, L., Baban, A., Kachaeva, M., … Terzic, N. (2014). Adverse childhood experiences and associations with health-harming behaviours in young adults: surveys in eight eastern European countries. *Bulletin World Health Organization, 4*(92), 641-655.

Bellis, M. A., Lowey, H., Leckenby, N., Hughes, K., & Harrison, D. (2014). Adverse childhood experiences: Retrospective study to determine their impact on adult health behaviours and health outcomes in a UK population. *Journal of Public Health, 36*(1), 81-91.

Benjet, C., Borges, G., & Medina-Mora, M. E. (2010). Chronic childhood adversity and onset of psychopathology during three life stages: Childhood, adolescence, and adulthood. *Journal of Psychiatric Research, 44*, 732-740. doi: 10/1016/j.jpsychires.2010.01.004

Bielas, H., Barra, S., Skrivanek, C., Aebi, M., Steinhausen, H-C., Bessler, C., & Plattner, B. (2016). The associations of cumulative adverse childhood experiences and irritability with mental disorders in detained male adolescent offenders. *Child and Adolescent Psychiatry and Mental Health, 10*(34), 1-10. doi: 10.1186/s13034-016-0122-7

Bjorkenstam, C., Bjorenstam, E., Ljung, R., Vinnerijung, B., & Tubvlad, C. (2013). Suicidal behavior among delinquent former child welfare clients. *European Child & Adolescent Psychiatry, 22*(6), 349-355. doi: 10.1007/s00787-012-0372-8

Bourgeois, F. T., Shannon, M. W., Valim, C., Mandl, K. D. (2010). Adverse drug events in the outpatient setting: An 11-year national analysis. *Pharmacoepidemiology Drug Safety, 19*, 901–910.

Brockie, T. N., Dana-Sacco, G., Wallen, G. R., Wilcox, H. C., & Campbell, J. C. (2015). The relationship of adverse childhood experiences to PTSD, depression, poly-drug use and suicide attempt in reservation-based Native American adolescents and young adults.

American Journal of Community Psychology, 55, 411-421. doi: 10.1007/s10464-015-9721-3

Brown, D. W., Anda, R. F., Felitti, V. J., Edwards, V. J., Malarcher, A. M., Croft, J. B., & Giles, W. H. (2010). Adverse childhood experiences are associated with the risk of lung cancer: A prospective cohort study. *BMC Public Health, 10*(20), 1-12. doi: 10.1186/1471-2458-10-20

Brown, N. M., Brown, S. N., Briggs, R. D., German, M., Belamarich, P. F., & Oyeku, S. O. (2017). Associations between adverse childhood experiences and ADHD diagnosis and severity. *Academic Pediatrics, 17*(4), 349-355.

Buckley, P., Citrome, L., Nichita, C., & Vitacco, M. (2011). Psychopharmacology of aggression in schizophrenia. *Schizophrenia Bulletin, 37*(5), 930-936. doi: 10.1093/schbul/sbr104

Burgess, C., Holman, C., & Satti, A. (2005). Adverse drug reactions in older Australians, 1981–2002. *Medical Journal of Australia, 182*, 267–270.

Campbell, N., Boustani, M., Limbil, T., Ott, C., Fox, C., Maidment, I., … Gulati, R. (2009). The cognitive impact of anticholinergics: A clinical review. *Clinical Interventions in Aging*, *4*, 225–233.

Campbell, J. A., Walker, R. J., & Egede, L. E. (2016). Associations between adverse childhood experiences, high-risk behaviors, and morbidity in adulthood. *American Journal of Preventive Medicine, 50*(3), 344-352.

Caprara, G. V., Cinanni, V., D'Imperio, G., Passerini, S., Renzi, P., & Travaglta, G. (1985). Indicators of impulsive aggression: Present status of research on irritability and emotional susceptibility scales. *Personality and Individual Differences, 6*(6), 665-674. doi: 10/1016/0191-8869(85)90077-7

Carnahan, R. M., Lund, B. C., Perry, P. J., & Chrischilles, E. A. (2006). Increased risk of extrapyramidal side-effect treatment associated with atypical antipsychotic polytherapy. *Acta Psychiatrica Scandinavica, 113*(2), 135–141. doi: 10.1111/j.1600-0447.2005.00589.x

Cosano, G., Manuela, G., Ussai, S., Giorgini, T., Biasutti, E., Barbone, F., & Pisa, F. E. (2016). Polypharmacy ad the use of medications in inpatients with acquired brain injury during post-acute rehabilitation: A cross-sectional study. *Brain Injury, 30*(3), 353-362. doi: 10.3109/02699052.2015.1118767

Centers for Disease Control and Prevention. (2013). Adverse childhood experiences (ACEs). Retrieved from http://www.cdc.gov/violenceprevention/acestudy/index.html

Centers for Disease Control and Prevention. (2016). *Child abuse and neglect: Data sources.* Retrieved from http://www.cdc.gov/violenceprevention/childmaltreatment/datasources.html

Chapman, D. P., Dube, S. R., & Anda, R. F. (2007). Adverse childhood events as risk factors for negative mental health outcomes. *Psychiatric Annals, 37*(5), 359-364.

Chapman, D. P., Whitfield, C. L., Felitti, V. J., Dube, S. R., Edwards, V. J., & Anda, R. F. (2004). Adverse childhood experiences and the risk of depressive disorders in adulthood. *Journal of Affective Disorders, 82*(2), 217-225. doi: 10.1016/j.jad.2003.12.013

Chartier, M. J., & Walker, J. R. (2009). Health risk behaviors and mental health problems as mediators of the relationship between childhood abuse and adult health. *American Journal of Public Health, 99*(5), 847-854. doi: 10.2105/ajph.2007.122408

Christiaens, I., Hegadoren, K., & Olsen, D. M. (2015). Adverse childhood experiences are associated with spontaneous preterm birth: A case-control study. *BMC Medicine, 13*,

124-133. doi: 10.1186/s12916-015-0353-0

Danese, A., & Tan, M. (2014). Childhood maltreatment and obesity: Systematic review and meta-analysis. *Molecular Psychiatry, 19*, 544-554.

de las Cuevas, C. & Sanz, E. (2005). Polypsychopharmacy: A frequent and debatable practice in psychiatric inpatients. *Journal of Clinical Psychopharmacology, 25*(5), 510-512.

Doan, J., Zakrewski-Jakubiak, H., Roy, J., Turgeon, J., & Tannenbaum, C. (2013). Prevalence and risk of potential cytochrome p450—mediated drug-drug interactions in older hospitalized patients with polypharmacy. *Annals of Pharmacotherapy, 47*, 324–332.

Dong, M., Anda, R. F., Felitti, V. J., Dube, S. R., Williamson, D. F., Thompson, T. J., … & Giles, W. H. (2004). The interrelatedness of multiple forms of childhood abuse, neglect, and household dysfunction. *Child Abuse & Neglect, 28*, 771-784. doi: 10.1016/j.chiabu.2004.01.008

Dong, M., Dube, S. R., Felitti, V. J., Giles, W. H., & Anda, R. F. (2003). Adverse childhood experiences and self-reported liver disease: New insights into the causal pathway. *Archives of Internal Medicine, 163*, 1949-1956.

Douglas, K. R., Chan, G., Gelernter, J., Arias, A. J., Anton, R. F., Weiss, R. D., … Kranzler, H. R. (2010). Adverse childhood events as risk factors for substance dependence: Partial mediation by mood and anxiety disorders. *Addictive Behaviors, 35*(1), 7-13. doi: 10.1016/j.addbeeh.2009.07.004

Draper, B., Pfaff, J. J., Pirkis, J., Snowdon, J., Lautenschlager, N. T., Wilson, I., & Almeida, O. P. (2008). Long-term effects of childhood abuse on the quality of life and health of older people: Results from the depression and early prevention of suicide in general practice project. *Journal of the American Geriatrics Society, 56*(2), 262-271.

Dube, S. R., Fairweather, D., Pearson, W. S., Felitti, V. J., Anda, R. F., & Croft, J. B. (2009). Cumulative childhood stress and autoimmune diseases in adults. *Psychosomatic Medicine, 71*, 243-250.

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 Experience study. *Pediatrics, 111*(3), 564-572. doi: 10/1542/peds.111.3.564

Dube, S. R., Miller, J. W., Brown, D. B., Giles, W. H., Felitti, V. J., Dong, M., & Anda, R. F. (2006). Adverse childhood experiences and the association with ever using alcohol and initiating alcohol use during adolescence. Journal of Adolescent Health, 38(4), e1-e10.

Dudeck, M., Sosic-Vasic, Z., Otte, S., Rasche, K., Leichauer, K., Tippelt, S., … Streb, J. (2016). The association of adverse childhood experiences and appetitive aggression with suicide attempts and violent crimes in male forensic psychiatry inpatients. *Psychiatry Research, 240*, 352-357. doi: 10.1016/j.psychres.2016.04.073

Duke, N. N., Pettingell, S. L., McMorris, B. J., & Borowsky, I. W. (2010). Adolescent violence perpetration: Associations with multiple types of adverse childhood experiences. *Pediatrics, 125*(4). doi:10.1542/peds.2009-0597

Dwyer, L. L., Han, B., Woodwell, D. A., & Rechtsteiner, E. A. (2010). Polypharmacy in nursing home residents in the United States: Results of the 2004 National Nursing Home Survey. *American Journal of Geriatric Polypharmacy, 8*(1), 63-72. doi: 10/1016/j.amjopharm.2010.01.001

Edwards, V. J., Fivush, R., Anda, R. F., Felitti, V. J., & Nordenberg, D. F. (2001). Autobiographical memory disturbances in childhood abuse survivors. *Journal of*

Aggression, Maltreatment, & Trauma, 4(2), 247-263. doi: 10.1300/J146v04n02.11

Felitti, V. J. (2009). Adverse childhood experiences and adult health. *Academic Pediatrics, 9*(3), 131-132.

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.

Food and Drug Administration. (2016). Drug development and drug interactions. Retrieved from https://www.fda.gov/drugs/developmentapprovalprocess/development resources/druginteractionslabeling/ucm080499.htm

Fontanella, C. A., Bridge, J. A., & Campo, J. V. (2009). Psychotropic medication changes, polypharmacy, and the risk of early readmission in suicidal adolescent inpatients. Annals of Pharmacotherapy, 43(12), 1939-1947. doi: 10.1345/aph.1M326

Ford, E. S., Anda, R. F., Edwards, V. J., Perry, G. S., Zhao, G., Chaoyang, L., & Croft, J. B. (2011). Adverse childhood experiences and smoking status in five states. *Preventive Medicine, 53*, 188-193. doi: 10.1016/j.ypmed.2011.06.015

Fornaro, M., de Berardis, D., Koshy, A. S., Perna, G., Valchera, A., Vancompfort, D., & Stubbs, B. (2016). Prevalence and clinical features associated with bipolar disorder polypharmacy: A systematic review. *Neuropsychiatric Disease and Treatment, 12*, 719-735.

Fox, B. H., Perez, N., Cass, E., Baglivio, M. T., & Epps, N. (2015). Trauma changes everything: Examining the relationship between adverse childhood experiences and serious, violent, and chronic juvenile offenders. *Child Abuse and Neglect, 46*, 163-173.

Fried, T. R., O'Leary, J., Towle, V., Goldstein, M. K., Trentalange, M., & Martin, D. K. (2014). Health outcomes associated with polypharmacy in community-dwelling older adults: A systematic review. *Journal of American Geriatric Society, 62*, 2261-2272. doi: 10.1111/jgs.13153

Fuller-Thomson, E., & Lewis, D.A. (2015). The relationship between early adversities and attention-deficit/hyperactivity disorder. *Child Abuse & Neglect, 47*, 94-101. doi:10.1016/j.chiabu.2015.03.005

Gallego, J. A., Bonetti, J., Zhang, J., Kane, J. M., & Correll, C. U. (2012). Prevalence and correlates of antipsychotic polypharmacy: A systematic review and meta-regression of global and regional trends from the 1970s to 2009. *Schizophrenia Research, 138*(1), 18-28.

Gilbert, L. K., Breiding, M. J., Merrick, M. T., Thompson, W. W., Ford, D. C., Dhingra, S. S., & Parks, S. E. (2015). Childhood adversity and adult chronic disease: An update from ten stated and the District of Columbia, 2010. (2015). *American Journal of Preventive Medicine, 48*(3), 345-349. doi: 10.1016/j.amepre.2014.09.006

Gnjidic, D., Tinetti, M., & Allore, H. G. (2017). Assessing medication burden and polypharmacy: finding the perfect measure. *Expert Review of Clinical Pharmacology*, *10*(4), 345–347. doi: 10.1080/17512433.2017.1301206

Gomez, C., Vega, S., Bermejo-Pareja, F., Medrano, M. J., Louis, E., & Benito-Leon, J. (2014). Polypharmacy in the elderly: A marker of increased mortality in a population-based prospective study (NEDICES). *Gerontology, 61*(4), 301-309. doi: 10.1159/000365328

Grubaugh, A. L., Zinzow, H. M., Paul, L., Egede, L. E., & Frueh, B. C. (2011). Trauma exposure and posttraumatic stress disorder in adults with severe mental illness: A critical review. *Clinical Psychology Review, 31*(6), 883-899. doi: 10.1016/j.cpr.2011.04.003

Gunstad, J., Paul, R. H., Spitznagel, M. B., Cohen, R. A., Williams, L. M., Kohn, M., & Gordon, E. (2006). Exposure to early life trauma is associated with adult obesity. *Psychiatry Research, 142*, 31-37. doi: 10/1016/j.psychres.2006.11.007

Guthrie, B., Makubate, B., Hernandez-Santiago, V., & Dreischulte, T. (2015). The rising tide of polypharmacy and drug-drug interactions: population database analysis 1995–2010. *BMC Medicine*, *13*, 74. doi: 10.1186/s12916-015-0322-7

Haider, S. I., Johnell, K., Weitoft, G. R., Thorslund, M., & Fastborn, J. (2009). The influence of educational level on polypharmacy and inappropriate drug use: A register-based study of more than 600,000 older people. *Journal of the American Geriatric Society, 57*(1), 62-69. doi: 10.1111/j.1532-5415.2008.02040.x

Hilton, N. Z., Ham, E., & Green, M. M. (2016). Adverse childhood experiences and criminal propensity among intimate partner violence offenders. Journal of Interpersonal Violence. doi: 10/1177/0886260516674943

Janssen, B., Weinmann, S., Berger, M., & Gaebel, W. (2004). Validation of polypharmacy process measures in inpatient schizophrenia care. *Schizophrenia Bulletin, 30*(4), 1023-1033.

Jokanovic, N., Tan, E. C. K., Dooley, M. J., Kirkpatrick, C. M., & Bell, J. S. (2016). Prevalence and factors associated with polypharmacy in long-term care facilities: A systematic review. *Journal of American Medical Directors Association, 16*(6), 535e1-535e12. doi: 10.1016/j.jamda.2015.03.003

Joukamaa, M., Heliovaara, M., Knekt, P., Aromaa, A., Raitasalo, R., & Lehtinen, V. Schizophrenia, neuroleptic medication and mortality. *British Journal of Psychiatry, 188,* 122-127.

Jyrkka, J., Enlund, H., Korhonen, M. J., Sulkava, R., & Hartikainen, S. (2009). Polypharmacy status as an indicator of mortality in an elderly population. *Drugs & Aging, 26*(12), 1039-1048. doi: 10.2165/11319530-000000000-00000

Kajeepta, S., Gelaye, B., Jackson, C. L., & Williams, M. A. (2015). Adverse childhood experiences are associated with adult sleep disorders: A systematic review. *Sleep Medicine, 16*, 320-330.

Karadog, H., Orsel, S., Addoyunlu, S., Kahilogullari, A. K., Guriz, O., Turkcapar, H., Hatiloglu, U. (2012). Comparison of polypharmacy in schizophrenia and other psychotic disorders in outpatient and inpatient treatment periods: A naturalistic one year follw-up study. Bulletin of Clinical Psychopharmacology, 22(2), 130-138.

Kenny, D. (2013). *Mediation with dichotomous outcomes* [PDF document]. Retrieved from Online Link at Website: http://davidakenny.net/cm/mediate.htm

Kenny, D. (2018, September). *Mediation.* Retrieved from http://davidakenny.net/cm/mediate.htm#IE

Krakowski, M. I., Czobor, P., & Nolan, K.A. (2008). Atypical antipsychotics, neurocognitive deficits, and aggression in schizophrenic patients. *Journal of Clinical Psychopharmacology, 28*(5), 485–493.

Kelly-Irving, M., Lepage, B., Dedieu, D., Lacey, R., Cable, N., Bartley, M., … Delpierre, C. (2013). Childhood adversity as a risk for cancer: Findings from the 1958 British birth cohort study. *BMC Public Health, 13*(767), 1-13. doi: 10.1186/1471-2458-13-767

Koskenvuo, K. & Koskenvuo, M. (2014). Childhood adversities predict strongly the use of psychotropic drugs in adulthood: A population-based cohort study of 24,284 Finns. *Journal of Epidemiology and Community Health, 69*, 354-360. doi: 10.1136/jech-2014-204732

Kukreja, S., Kalra, G., Shah, N., & Shrivastava, A. (2013). Polypharmacy in psychiatry: A review. *Mens Sana Monographs*, *11*(1), 82–99. doi: 10.4103/0973-1229.104497

Lacasse, J. R. (2014). Antipsychotic polypharmacy at admission predicts extended length of stay among state hospital inpatients. *Australian and New Zealand Journal of Psychiatry, 48*(11), 1065. doi: 10.1177/0004867414535674

Langan, J. & Shajahan, P. (2010). Antipsychotic polypharmacy: Review of mechanisms, mortality and management. *Psychiatrist, 34*, 58-62.

Leahy, L. G. (2017). Off-label prescribing and polypharmacy: Minimizing the risks. *Journal of Psychosocial Nursing and Mental Health Services, 55*(2), 17-22. doi: 10.3928/02793695-20170210-02

Levenson, J. (2013). Incorporating trauma-informed care into evidence-based sex offender treatment. *Journal of Sexual Aggression*, 1-14. doi:10.1080/13552600.2013.861523.

Levenson, J. S., Willis, G. M., & Prescott, D. S. (2014). Adverse childhood experiences in the lives of male sex offenders: Implications for trauma-informed care. *Sexual Abuse: A Journal of Research and Treatment,* 1-20. doi: 10.1177/1079063214535819

Levenson, J. S., Willis, G. M., & Prescott, D. S. (2015). Adverse childhood experiences in the lives of female sex offenders. *Sexual Abuse: A Journal of Research and Treatment, 27*(3), 258-283.

Lieberman, J. A. (2004). Managing Anticholinergic Side Effects. *Primary Care Companion to The Journal of Clinical Psychiatry*, *6*(suppl 2), 20–23.

Londono, A., Ballester, P., Martinez, E., Javaloyes, A., Planelles, B., Perez, A., & Peiro, A. (2016). Comorbidities as predictor of polypharmacy in autism spectrum disorder. *Child and Adolescent Disorders and Treatment – Treatment (Clinical), P.7.d.*(004), S730-S731.

Mace, S. & Taylor, D. (2015). Reducing the rates of prescribing high-dose antipsychotics and polypharmacy on psychiatric inpatient and intensive care units: Results of a 6-year quality improvement programme. *Therapeutic Advances in Psychopharmacology, 5*(1), 4-12. doi: 10.1177/2045125314558054

Madan, A., Oldham, J. M., Gonzalez, S., & Fowler, J. C. (2015). Reducing adverse polypharmacy in patients with borderline personality disorder: An empirical case study. *Primary Care Companion CNS Disorders, 17*(4). doi: 10.4088/PCC.14m01760

Marie-Mitchell, A. & O'Connor, T. G. (2013). Adverse childhood experiences: Translating knowledge into identification of children at risk for poor outcomes. *Academic Pediatrics, 13*(1), 14-19.

McLaughlin, K. A., Green, J. G., Gruber, M. J., Sampson, N. A., Zaslavsky, A. M., & Kessler, R. C. (2010). Childhood adversities and adult psychiatric disorders in the National Comorbidity Survey Replication II: Associations with persistence of DSM-IV disorders. *Archives of General Psychiatry, 67*(2), 124-132. doi: 10.1001/archgenpsychiatry.2009.187

Medeiros-Souza, P., dos Santos-Neto, L. L., Kusano, L. T. E., & Pereira, M. G. (2007). Diagnosis and control of polypharmacy in the elderly. *Revista Saude Publica, 41*(6), 1049-1053.

Mersky, J. P., Topitzes, J., & Reynolds, A. J. (2013). Impacts of adverse childhood experiences on health, mental health, and substance use in early adulthood: A cohort study of an urban, minority sample in the U.S. *Child Abuse & Neglect, 13*, 917-925. doi: 10.1016/j.chiabu.2013.07.011

Messina, N., Grella, C., Burdon, W., & Prendergast, M. (2007). Childhood adverse events and current traumatic distress: A comparison of men and women drug-dependent prisoners. *Criminal Justice and Behavior, 34*(11), 1385-1401. doi: 10.1177/0093854807305150

Millan, M. J. (2014). On 'polypharmacy' and multi-target agents, complementary strategies for improving the treatment of depression: A comparative appraisal. *International Journal of Neuropsychopharmacology, 17*, 1009-1037. doi: 10.1017/S1461145712001496

Moller, H. J., Seemuller, F., Schennach-Wolff, R., Stubner, S., Ruther, E., & Grohmann, R. (2014). History, background, concepts and current use of comedication and polypharmacy in psychiatry. *International Journal of Neuropsychopharmacology, 17*, 983-996. doi: 10.1017/S1461145713000837

Monnat, S. M. & Chandler, R. F. (2015). Long-term physical health consequences of adverse childhood experiences. The Sociology Quarterly, 56, 723-752. doi: 10.1111/tsq.12107

Moriarty, F., Hardy, C., Bennett, K., Smith, S. M., & Fahey, T. (2015). Trends and interaction of polypharmacy and potentially inappropriate prescribing in primary care over 15 years in Ireland: A repeated cross-sectional study. *BMJ Open, 5*. doi: 10.1136/bmjopen-2015-008656

Morrissette, D. A. & Stahl, S. M. (2014). Treating the violent patient with psychosis or impulsivity utilizing antipsychotic polypharmacy and high-dose monotherapy. *CNS Spectrum, 19*, 439-448. doi: 10.1017/S1092852914000388

Medical Directors Council and State Medicaid Directors. (2001). *National Association of State Mental Health Program Directors: Technical report on psychiatric polypharmacy.* Alexandria, VA.

Naples, J. G., & Hajjar, E. R. (2016). Multimorbidity and polypharmacy In Stegemann (Ed.), *Developing drug products in an aging society*, AAPS Advances in the Pharmaceutical Sciences Series 24 (pp. 549-561). doi: 10.1007/978-3-319-43099-7_25

National Association of State Mental Health Program Directors. (2001). Technical report on psychiatric polypharmacy.

Newsom (2016). Psy 510/610: Categorical Data Analysis [PDF document]. Retrieved from http://web.pdx.edu/~newsomj/cdaclass/ho_mediation.pdf

Odgers, C. L., Moffitt, T. E., Broadbent, J. M., Dickson, N., Hancox, R. J., Harrington, H., … Caspi, A. (2008). Female and male antisocial trajectories: From childhood origins to adult outcomes. *Developmental Pychopathology, 20*(2), 673-716. doi:10.1017/S0954579408000333.

Office of Disease Prevention and Health Promotion. (2017). Adverse drug events. Retrieved from https://health.gov/hcq/ade.asp

Onder, G., Petrovic, M., Tangiisuran, B., Meinardi, M. C., Markito-Notenboom, W. P., Somers, A., … van der Cammen, T. J. (2010). Development and validation of a score to assess risk of adverse drug reactions among in-hospital patients 65 years or older: The GerontoNet ADR risk score. *Archives of Internal Medicine, 170*, 1142–1148. doi: 10.1001/archinternmed.2010.153

Peselow, E. D., Naghdechi, L., Pizano, D., & IsHak, W. W. (2016). Polypharmacy in maintenance of bipolar disorder. *Clinical Neuropharmacology, 39*(3), 132-134. doi:

10.1097/WNF.0000000000000147

Pierre, J. M. (2005). Extrapyramidal symptoms with atypical antipsychotics: Incidence, prevention, and management. *Drug Safety, 28*(3), 191-208. doi: 10.2165/00002018-20058030-00002

Pilowsky, D. J., Keyes, K. M., & Hasin, D. S. (2009). Adverse childhood events and lifetime alcohol dependence. *American Journal of Public Health, 99*(2), 258-263.

Preskon, S. H. & Lacey, R. L. (2007). Polypharmacy: When is it rational? *Journal of Psychiatric Practice, 13*(2), 97-105. doi: 10.1097/01.pra.0000265766.25495.3b

Pringsheim, T., Doja, A., Belanger, S., Patten, S., & The Canadian Alliance for Monitoring Effectiveness and Safety of Antipsychotics in Children (CAMESA) guideline group. (2011). Treatment recommendations for extrapyramidal side effects associated with second-generation antipsychotic use in children and youth. *Paediatrics & Child Health*, *16*(9), 590–598.

Rambhade, S., Chakarborty, A., Shrivastava, A., Patil, U. K., & Rambhade, A. (2012). A survey on polypharmacy and use of inappropriate medications. *Toxicology International, 19*(1), 68-73. doi: 10/4103/0971-6580.94506

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. doi: 10.7812/TPP/12-072

Rosenberg, S. D., Lu, W., Mueser, K. T., Jankowski, M. K., & Cournos, F. (2007). Correlates of adverse childhood events among adults with schizophrenia spectrum disorders. *Psychiatric Services, 58*(2), 245-253.

Rytilä-Manninen, M., Lindberg, N., Haravuori, H., Kettunen, K., Marttunen, M., Joukamaa, M.,

& Fröjd, S. (2014). Adverse childhood experiences as risk factors for serious mental disorders and inpatient hospitalization among adolescents. *Child Abuse and Neglect, 38*, 2021-2032.

Sacco, K. A., Head, C. A., Vessicchio, J. C., Easton, C. J., Prigerson, H. G., & George, T. P. (2007). Adverse childhood experiences, smoking and mental illness in adulthood: A preliminary study. *Annual Clinical Psychiatry, 19*(2), 89-97. doi: 10/1080/10401230701334762

Schalinski, I., Teicher, M. H., Nischk, D., Hinderer, E., Muller, O., & Rockstroh, B. (2016). Type and timing of adverse childhood experiences differentially affect severity of PTSD, dissociative and depressive symptoms in adult inpatients. *BMC Psychiatry, 19*(16), 295. doi: 10/1186/s12888-016-1004-5

Schilling, E., Aseltine, R, Jr, & Gore, S. (2007). Adverse childhood experiences and mental health in young adults: A longitudinal survey. *BMC Public Health, 7*, 30. doi:10.1186/1471-2458-7-30

Scott, I. A., Hilmer, S. N., Reeve, E., Potter, K., Le Couteur, D., Rigby, D., … Martin, J.H. (2015). Reducing inappropriate polypharmacy: The process of deprescribing. *JAMA Internal Medicine,* 175(5), 827–834. doi:10.1001/jamainternmed.2015.0324

Sinnott, C., McHugh, S., Fitzgerald, A. P., Bradley, C. P., & Kearney, P. M. (2015). Psychosocial complexity in multimorbidity: The legacy of adverse childhood experiences. *Family Practice, 32*(3), 269-275. doi: 10.1093/fampra/cmv016

Spidel, A., Lecomte, T., Greaves, C., Sahlstrom, K., & Yuille, J. C. (2010). Early psychosis and aggression: Predictors and prevalence of violent behavior amongst individuals with early onset psychosis. *International Journal of Law and Psychiatry, 33*, 171-176.

Spinhoven, P., Elzinga, B. M., Hovens, J. G. F. M., Roelofs, K., Zitman, F. G., van Oppen, P., & Penninx, B. W. J. H. (2010). The specificity of childhood adversities and negative life events across the life span to anxiety and depressive disorder. *Journal of Affective Disorders, 126*, 103-112. doi: 10.1016/j.jad.2010.02.132

Stahl, S. M. (2014). Deconstructing violence as a medical syndrome: Mapping psychotic, impulsive, and predatory subtypes to malfunctioning brain circuits. *CNS Spectrum, 19*(5), 357-365. doi: 10.1017/S1092852914000522

Stinson, J. D., Quinn, M. A., & Levenson, J. S. (2016). The impact of trauma on the onset of mental health symptoms, aggression, and criminal behavior in an inpatient psychiatric sample. *Child Abuse & Neglect, 61*, 13-22. doi: 10.1016/j.chiabu.2016.09.005

Stoltenborgh M., Bakermans-Kranenburg M. J., Alink L. R. A., & van IJzendoorn M. H. (2015). The prevalence of child maltreatment across the globe: Review of a series of meta-analyses. *Child Abuse Rev., 24*(1), 37–50, doi: 10.1002/car.2353.

Stumbo, S. P., Yarborough, B. J. H., Paulson, R. I., & Green, A. (2015). The impact of adverse child and adult experiences on recovery from serious mental illness. *Psychiatric Rehabilitation Journal, 38*(4), 320-327. doi: 10/1037/prj0000141

Suoka, J. T., Suvisaari, J. M., Haukka, J. Korhonen, P., & Tiihonen, J. (2013). Description of long-term polypharmacy among schizophrenia outpatients. *Social Psychiatry and Psychiatric Epidemiology, 48*, 631-638. doi: 10.1007/s00127-012-0586-6

Swanson, J. W., Swartz, M. S., van Dorn, R. A., Volavka, J., Monahan, J., Stroup, T. S., … Lieberman, J. A. (2008). Comparison of antipsychotic medication effects on reducing violence in people with schizophrenia. *British Journal of Psychiatry, 193*(1), 37-43. doi: 10.1192/bjp.bp.107.042630

Tapp, J., Perkins, D., Warren, F., Fife-Schaw, C. & Moore, E. (2013). A critical analysis of clinical evidence from high secure forensic inpatient services. *International Journal of Forensic Mental Health*, 12, 1, 68-82.

Turner, H.A., Finkelhor, D., Shattuck, A., & Hamby, S. (2012). Recent victimization exposure and suicidal ideation in adolescents. *Archives of Pediatrics & Adolescent Medicine, 162*(12), 1149-1154. doi:10.1001/archpediatrics.2012.1549

Varese, F., Smeets, F., Drukker, M., Lieverse, R., Lataster, T., Viechtbauer, W., … Bentall, R. P. (2012). Childhood adversities increase the risk of psychosis: a meta-analysis of patient-control, prospective- and cross-sectional cohort studies. *Schizophrenia Bulletin, 38*, 661–71.

Viktil, K. K., Blix, H. S., Moger, T. A., & Reikvam, A. (2007). Polypharmacy as commonly defined is an indicator of limited value in the assessment of drug-related problems. *British Journal of Clinical Pharmacology*, *63*(2), 187–195. doi: 10.1111/j.1365-2125.2006.02744.x

Vyas, A., Pan, X. L., & Sambamoorthi, U. (2012). Multimorbidity and polypharmacy. *Values in Health, 15*(PHP26), A17-A18.

Waddington, J. L., Youssef, H. A., & Kinsella, A. (1998). Mortality in schizophrenia: Antipsychotic polypharmacy and absence of adjunctive anticholinergics over the course of a 10-year prospective study. *British Journal of Psychiatry, 173*, 325-329.

Walsh, E. G., & Cawthon, S. W. (2014). The mediating role of depressive symptoms in the relationship between adverse childhood experiences and smoking. *Addictive Behaviors, 39*, 1471-1476.

Whitfield, C. L., Anda, R. F., Dube, S. R., & Felitti, V. J. (2003). Violent childhood experiences and the risk of intimate partner violence in adults: Assessment in a large health maintenance organization. *Journal of Interpersonal Violence, 18*(2), 166-185. doi: 10.1177/0886260502238733

Whitfield, C. L., Dube, S. R., Felitti, V. J., & Anda, R. F. (2005). Adverse childhood experiences and hallucinations. *Child Abuse & Neglect, 29*, 797-810. doi: 10.1016/j.chiabu.2005.01.004

Wilson, H. W., & Widom, C. S. (2008). An examination of risky sexual behavior and HIV in victims of child abuse and neglect: A 30-year follow-up. *Health Psychology, 27*(2), 149-158. doi: 10.1037/0278-6133.27.2.149

Wu, N. S., Schairer, L. C., Dellor, E., & Grella, C. (2010). Childhood trauma and health outcomes in adults with comorbid substance abuse and mental health disorders. *Addictive Behaviors, 35*, 68-71.

Wunderlink, L., Nieboer, R. M., Wiersma, D., Sytema, S., & Nienhuis, F. J. (2013). Recovery in remitted first-episode psychosis at 7 years of follow-up of an early dose reduction/discontinuation or maintenance treatment strategy: Long-term follow-up of a 2-year randomized clinical trial. *JAMA Psychiatry, 70*(9), 913-920.

Young, S., Misch, P., Collins, P., & Gudjonsson, G. (2011). Predictors in institutional behavioral disturbance and offending in the community among young offenders. *Journal of Forensic Psychiatry and Psychology, 22*(1), 72-86. doi: 10.1080/14789949.2010.495991

VITA

CARRIE LEMAY

Education:	B.A. Psychology: Minor in Chemistry, University of Mississippi, Oxford, Mississippi 2009 B.S. Biological Sciences, University of Mississippi, Oxford, Mississippi 2009 M.S. Psychology, University of Tennessee at Chattanooga, Chattanooga, Tennessee 2014 Ph.D. Psychology, concentration in Clinical Psychology, East Tennessee State University, Johnson City, Tennessee 2019
Professional Clinical Experiences:	Graduate Clinician, Behavioral Health and Wellness Clinic; Johnson City, Tennessee 2016 – 2018 Graduate Clinician, Cherokee Health Systems; Morristown, Tennessee 2016 – 2017 Graduate Clinician, ETSU Family Medicine Associates; Johnson City, Tennessee 2017 – 2018 Pre-Doctoral Internship, Memphis Veterans Affairs Medical Center – Clinical Health Emphasis (APA Accredited); Memphis, Tennessee 2018 – 2019
Professional Experiences:	Instructor, University of Mississippi, College of Arts and Sciences, 2009 – 2011 Instructor & Graduate Assistant, University of Tennessee at Chattanooga, College of Arts and Sciences, 2012 – 2014 Graduate Assistant, East Tennessee State University, College of Arts and Sciences, 2014 – 2016 Instructor, East Tennessee State University, College of Arts and Sciences, 2015 – 2016
Publications:	Cunningham, C.J.L., LeMay, C.C., Sarnosky, K.M., & Anderson, A. (2014). Addressing response shift bias: A cultural competence evaluation example. In L.C. Caputi (Ed.), *Innovations in Nursing Education: Building the Future of Nursing, Volume 2* (39-44). Washington, DC: National League for Nursing.

Oral Presentations:

LeMay, C.C., Polaha, J., & Williams, A. (2017, September). *Warm handoffs: The good, the awkward, and the ugly.* ETSU Family Medicine Associates. Johnson City, Tennessee.

LeMay, C.C. & Russell, E. (2017, August). *Hospital to home – Transitions of care team integrated approach.* James H. Quillen College of Medicine. Johnson City, Tennessee.

LeMay, C.C. & Stinson, J.D. (2017, April). *Polypharmacy: Is it just too much?* Appalachian Student Research Forum. Johnson City, Tennessee.

LeMay, C.C., Cantrell, P., & Stinson, J.D. (2016, May). *End of life care and the role of the psychologist.* Appalachian Student Research Forum. Johnson City, Tennessee.

LeMay, C.C. & Stinson, J.D. (2015, October). *The role of traumatic brain injury in sexual offending.* Association for the Treatment of Sexual Abusers. Montreal, Canada.

LeMay, C.C. (2015, May). *Indiscriminate behavior: Intellectual and developmental disabilities.* East Tennessee State University 2015 Data Blitz. Johnson City, Tennessee.

Honors and Awards:

Research Presentation Award – Tennessee Psychological Association, 2013

Association of Chemoreception Sciences Student Award, 2013

Provost Student Research Award, 2013 – 2014

Outstanding Research Award – University of Tennessee at Chattanooga, 2014

Outstanding Graduate Student Award – University of Tennessee at Chattanooga, 2014

Poster Presentation Award – Appalachian Student Research Forum, 2015

Graduate Student Association of Psychology Merit Award – Research, 2016

Poster Presentation Award – Appalachian Student Research Forum, 2016

Association of the Treatment of Sexual Abusers Student Award, 2016

Outstanding Poster Award – Association for the Treatment of Sexual Abusers, 2017

Poster Presentation Award – Appalachian Student Research Forum, 2018