Title

The Association Between Childhood Poverty and Adversity and the Likelihood of Experiencing Co-occurring Psychiatric and Substance Use Disorders

Author

vanDraanen Earwaker, Jenna Marie

Publication Date

2017

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

The Association Between Childhood Poverty and Adversity and the Likelihood of Experiencing Co-occurring Psychiatric and Substance Use Disorders

A dissertation submitted in partial satisfaction of the requirements for the degree of

Doctor of Philosophy in Community Health Sciences

by

Jenna Marie vanDraanen Earwaker

2017

ABSTRACT OF THE DISSERTATION

The Association Between Childhood Poverty and Adversity

and the Likelihood of Experiencing Co-occurring

Psychiatric and Substance Use Disorders

by

Jenna Marie vanDraanen Earwaker

Doctor of Philosophy in Community Health Sciences

University of California, Los Angeles, 2017

Professor Carol S. Aneshensel, Chair

Co-occurring disorder (COD) refers to concurrent psychiatric and substance use disorders (SUD). Compared to those with a single disorder, individuals with COD often require more complex treatment, have poorer health outcomes, and incur higher treatment costs. Researchers have extensively studied both the high lifetime prevalence and age of onset for psychiatric disorders and SUD independently, but little is known about the social antecedents of COD, especially how these antecedents vary by race/ethnicity and gender.

I expect the antecedents do not behave universally, though they are currently treated that way. Guided by the Stress Process Model, the Theory of Fundamental Causes, and the Life Course Perspective, this dissertation aims to better understand the role of childhood poverty and childhood adversity in the occurrence of COD for males and females, and for different racial/ethnic groups. This dissertation employs a secondary analysis of existing community-based survey data recorded in the National Epidemiologic Survey of Alcohol and Related Conditions III.

Using multinomial logistic regression with a four-category variable for disorder (categories: COD, SUD only, psychiatric disorder only, no disorder), on a bivariate level, childhood poverty is associated with COD, however, with the addition of all other covariates there is no longer an association between poverty and COD. Childhood adversities are strongly associated with COD, net of other factors, in all of the models estimated.

There are clear race/ethnicity differences in prevalence of disorder when COD is studied in the whole population. For COD relative to no disorder, Blacks, Asian Americans, and Hispanics, are all approximately half as likely as Whites to have COD, net of other factors. There are no conditional race/ethnicity relationships for COD. There are, however, gender differences in both disorder prevalence and the associations between childhood poverty and COD as well as childhood adversity and COD. Childhood poverty is associated with COD in opposite directions for males and females: for males it increases the relative risk ratio of COD compared to SUD, and for females it decreases the relative risk for this same comparison. This study found no moderation of the childhood poverty and COD relationship by number of adversities in the regressions conducted.

Conducting a survival analysis with only respondents who have at least one disorder indicates that having psychiatric disorder compared to having SUD is associated with a 36% increase in the hazard ratio of subsequently developing COD overall. The significant conditional relationship between disorder sequence and gender shows that hazard of co-occurrence with a psychiatric disorder is higher for males than females. On the contrary, the hazard of co-occurrence when one has SUD is higher for females than it is for males.

This research has clear public health relevance: above and beyond the genetic risk incurred by having a parent with a disorder, experiencing adverse events in childhood is

associated with COD. Efforts to help children and adolescents ameliorate the adversity they are exposed to are important and may be able to diminish the risk of COD associated with harmful early experiences.

The dissertation of Jenna Marie vanDraanen Earwaker is approved.

Dawn M. Upchurch

Todd M. Franke

Anne R. Pebley

Carol S. Aneshensel, Committee Chair

University of California, Los Angeles

2017

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VITA

Education

2009-2011 Master of Public Health, University of Toronto, Health Promotion

2004-2009 Bachelor of Science, University of Waterloo, Health Studies Co-op

Professional Experience

2014-2017 Graduate Student Researcher, UCLA, *California Centre for Population Research*

2009-2017 CEO and Principal Evaluator, Blink Evaluations, *Program and Policy Evaluation Consulting*

2014 Teaching Assistant, University of California, Los Angeles, *Health Policy and Management Department, Course: HPM422, Health Services Evaluation*

2011-2014 Research Coordinator, St. Michael's Hospital, *Centre for Research on Inner City Health and The Evaluation Centre for Complex Health Interventions*

2008-2011 Research Assistant, Sunnybrook Odette Cancer Centre, *Department of Pharmacy*

2010-2011 Teaching Assistant, University of Toronto, *Social Sciences Department, Course: HLTB03, Foundations in Health Studies*

2009 Research Assistant, University of Waterloo, *Health Studies and Gerontology, Tobacco Control*

Honors and Awards

2016 Phi Beta Kappa International Scholarship
2016 UCLA Graduate Summer Research Mentorship
2015 University Credit Union Scholarship
2015 Albert Schweitzer Fellowship
2014 CESEF Education Assistance Award
2013 UCLA Graduate Division Fellowship
2013 University of Waterloo Young Alumni Award Recipient
2013 CIHR Frederick Banting and Charles Best Doctoral Research Award (declined)
2009 CIHR Strategic Training in Public Health Policy Fellowship
2009 Ontario Graduate Scholarship

Peer-Reviewed Publications

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CHAPTER 1: BACKGROUND

1.1 Dissertation Overview

The overall goal of this study is to elucidate the role of childhood poverty and childhood stressors in the occurrence of co-occurring disorder (COD) for different racial/ethnic groups and for males and females. Chapter 1 reviews the current literature and articulates the significance of this study to the fields of mental health and addiction research by presenting evidence supporting the relevance of this investigation to these fields of research and to the serious social problem of COD. In Chapter 2, I present hypothesized associations between childhood poverty, childhood adversity, and COD relative to other disorder outcomes (i.e., psychiatric disorder only, substance use disorder (SUD) only, and no disorder). Chapter 2 also introduces the theories that guide this dissertation: the Life Course Perspective (Elder, 2003), the Stress Process Model (Pearlin et al., 1981), and the Theory of Fundamental Causes (Link & Phelan, 1995), and describes the conceptual model for this study. Data for this dissertation come from individuals who participated in Wave 3 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-III), a nationally-representative psychiatric epidemiological survey of adults in the United States. In Chapter 3, I present the research design and analytic methods applied to NESARC-III data to examine and describe relationships. In Chapters 4, 5, and 6, I detail the results from the analyses of the hypothesized relationships between childhood poverty, adversity, and COD, as well as the analyses related to sequential ordering and timing of disorder onset. In Chapter 4, I first present the results of the investigation of childhood adversity measures. Then I use multinomial logistic regression analysis to assess the factors that are differentially associated

with lifetime COD, lifetime SUD only, lifetime psychiatric disorder only, and no lifetime disorder. Chapter 5 examines the conditional relationships between childhood poverty and childhood adversity by race/ethnicity and by gender, and presents stratified models for males and females that clarify correlates of disorder outcomes for each gender. Chapter 6 assesses COD risk by presenting survival analyses of time from birth to COD and time between disorders. Chapter 7 includes an interpretation of the research findings, including strengths and limitations, as well as public health implications and suggestions for future research.

1.2 Introduction

Co-occurring disorder (COD) refers to the concurrence of psychiatric disorder[1] and SUD (SUD) (Drake et al., 1998) within an individual, and can affect as many as 50% of those who develop a single disorder (Kessler et al., 2005). Compared to those with a single disorder, individuals with COD often require more complex treatment that addresses both disorders, have poorer health outcomes, and incur higher treatment costs, accounting for over $360 billion in national health care expenditures (Tiet & Mausbach, 2007).

This chapter introduces the concept of co-occurring substance use and psychiatric disorders and reviews the research that has been done to date on this important issue. This review of the literature exposes the lack of knowledge about the antecedents of COD, as well as the uncertainty related to how these antecedents vary by race/ethnicity and gender. Then, I make the case for the importance of this study – which determines the influence of childhood poverty and childhood adversity on disorder outcomes specifically for males and females and for different racial/ethnic groups in the US population –and its vital contribution to the field.

[1] I refer to psychiatric disorders as a term encompassing all mental and emotional disorders, separated from the category of SUD (including drug and alcohol disorders).

Researchers have extensively studied both the high lifetime prevalence and age of onset for psychiatric disorders and SUD independently (Kessler et al., 2005), but little is known about the antecedents of COD, especially how these antecedents vary by race/ethnicity and gender. Gender differences in the development of COD have been given inadequate attention, despite evidence that women and men commonly develop different types of both psychiatric disorder and SUD (Kessler et al., 2005). Racial/ethnic differences in the antecedents of COD have also been overlooked to date, though it is apparent that racial/ethnic differences exist within the prevalence of COD (Kessler et al., 2005). Stressors, for example, are usually inversely associated with many disorders, yet paradoxically, both Hispanics and non-Hispanic Blacks exhibit either lower or similar rates of most disorders (Breslau et al., 2005; Breslau et al., 2006) than do non-Hispanic Whites while also recording higher exposure to stressful events (Paradies et al., 2015). Moreover, these gender and racial/ethnic identities and the social statuses they confer may intersect to produce complex disparities in COD: a possibility ignored in existing research on COD.

The antecedents of COD, previously under-examined with respect to gender and race/ethnicity, are also key correlates for this study, whose primary aim is to assess the roles of childhood poverty and childhood stressors[2] amongst various sub-groups of the population in the development of disorder. Such a study is both well-timed and well-positioned to add to the paucity of literature on how the early social determinants of co-occurring substance use and psychiatric disorder vary by gender and race/ethnicity.

[2] The terms childhood stressors and childhood adversities will be used interchangeably in this study to indicate adverse events and circumstances before age 18 (excluding the experience of childhood poverty)

This dissertation employs a secondary analysis of existing community-based survey data recorded in the National Epidemiologic Survey of Alcohol and Related Conditions III (NESARC-III) to assess the antecedents of the onset of COD as informed by the Life Course Perspective (Elder, 2003), the Stress Process Model (Pearlin et al., 1981), and the Theory of Fundamental Causes (Link & Phelan, 1995). The Life Course Perspective informs the inclusion of temporal elements and life stages into the research design for this study, whereas the Stress Process Model emphasizes the role of stressors in psychiatric disorders and SUD outcomes. The Theory of Fundamental Causes highlights the flexible resources available to those with privileged social statuses that confer health benefits, and provides the theoretical foundation for the gender and race hypotheses posited here. This dissertation employs the elaboration model (Aneshensel, 2013; Rosenberg, 1986) to test whether various types of childhood adversity intensify the relationship between childhood poverty and COD. The study also tests whether or not childhood poverty and childhood adversity have the same effects for all racial/ethnic groups, and for males and females.

The specific Aims of this study are:

- Aim 1: To determine if there is an association between childhood poverty, childhood stressors, and COD lifetime occurrence,
- Aim 2: To test if the effect of childhood poverty on lifetime COD is intensified by the experience of childhood stressors, and
- Aim 3: To test the associations between experiencing poverty and stressors in childhood and the timing of onset of lifetime COD.

I investigate lifetime COD defined as a condition in which an individual has two or more disorders, including at least one psychiatric disorder and at least one SUD, as they are defined in

Axis 1 of the *Diagnostic and Statistical Manual of the American Psychiatric Association, 5th Edition (DSM-5* American Psychiatric Association, 2013) at some point in their lives. While some definitions of COD require at least two disorders to be *simultaneously* present, I study lifetime COD in this dissertation. I choose to look at disorder co-occurrence throughout the lifetime without requiring explicit temporal overlap for three main reasons: 1) the literature is inconclusive on how close disorders need to be to each other in time to be considered overlapping, and what constitutes a period of remission; 2) looking at the co-occurrence of disorders over the life course is consistent with the theories I am drawing on that highlight the long reach of childhood stressors and the interplay of social factors throughout the lifetime; and 3) NESARC-III does not collect time and duration information for all disorders only timing and duration of: the first occurrence of each disorder, the most severe occurrence of each disorder, the most recent occurrence of each disorder, and every disorder happening in the year prior to data collection. Not all episodes of temporal co-occurrence can be identified in this dataset. Sensitivity testing with temporally-overlapping COD during the year prior to data collection, however, is possible and is presented in this dissertation.

1.3 Literature Related to the Dissertation

1.3.1 The Phenomenon of Co-occurring Disorder and its Significance

COD refers to concurrent psychiatric disorder and SUD (Drake et al., 1998), and is extremely common among people with either a psychiatric disorder or an SUD, affecting as many as 50% of adults with an existing disorder (Kessler et al., 2005). COD patients incur high treatment costs and account for a larger proportion of national health care expenditure than those with only one disorder (Tiet & Mausbach, 2007). There are several similar and overlapping

terms used to refer to COD, including *concurrent disorders* and *dual diagnosis.* COD remains difficult to diagnose and treat and, as a result, does not receive as much research attention as it otherwise might.

Four explanations for the existence of the phenomenon of COD have been hypothesized: 1) SUD causes stress and can lead to psychiatric disorder through maladaptive behavioral responses to this stress; 2) SUD is a form of self-medication adopted as a means of coping with symptoms of psychiatric disorder; 3) SUD and psychiatric disorder share a common etiology that may, in fact, cause both disorders, but do so independently from one another, and 4) psychiatric disorder and SUD maintain each other (Gregg, Barrowclough & Haddock, 2007). Few studies have thoroughly tested any of these four hypotheses. In addition, empirical evidence for both the overall causes of COD and for antecedents for different subgroups of the population is lacking (Crawford, Crome & Clancy, 2003).

Disentangling the symptoms of substance use and psychiatric disorders makes COD diagnosis challenging, complicating the creation of appropriate treatment plans. Individuals with COD often require treatment that accounts for certain situational complexities surrounding individuals with COD, who, compared with individuals with only psychiatric disorder, exhibit an increased likelihood of comparatively poorer health outcomes that include the exacerbation of psychiatric symptoms, medication non-adherence, an increase in aggressive behaviors, and increased numbers of hospital visits (Buckley, 2006; Tiet & Mausbach, 2007).

There is a structural divide between the treatment systems for mental health and substance use that presents challenges to integrated services (Grella 1996; Watkins et al., 2001). In addition, training programs typically prepare professionals to treat only one type of disorder (Newmann et al., 1998). Nonetheless, there is a push to bridge the divide between mental health

and substance use service systems and for professionals to become accustomed to expect comorbid SUD and psychiatric disorder as the norm in treatment rather than the exception (Minkoff, 2001). Although this expectation is overstated, as only 50% of all patients with a disorder will experience co-occurrence, it helps to make the case that substance use and psychiatric comorbidity is something that should be considered as a possible outcome, screened for routinely, considered in treatment planning for people who do experience COD. This study will help to bridge the gap between research on psychiatric disorder and SUD by assessing the prevalence of co-occurrence in relation to the presence of only one disorder, by analyzing how childhood factors make this co-occurrence more or less likely, and by showing temporal trends in the development of COD for those with an existing psychiatric disorder distinctly from those with existing SUD: all information which is currently missing at the population level. Further, this study builds on Minkoff's (2001) suggestion for treating co-occurrence as a normative expectation, by looking for psychiatric and substance use co-morbidity as a likely outcome for those who already have one disorder at the population level, and adds considerably to the evidence in the field of COD research by investigating COD in a large, recent, psychiatric epidemiology dataset.

1.3.2 Gender Differences in Co-occurring Disorder

Gender differences exist in both psychiatric and SUD prevalence: men are significantly more likely to develop SUD as well as personality/conduct disorders, whereas women are more likely to develop mood and anxiety disorders, such as depression (Kessler et al., 2005). A systematic review of the literature on COD (Najt et al., 2011) found that COD is more commonly associated with being male than female (Rounsaville et al., 1987; Goldberg et al., 1999; Davis et al., 2005). However, most of the studies reviewed were clinical samples and were disorder-

specific (e.g., studying alcohol and drug use with inpatients being treated for bipolar disorder, as Goldberg and colleagues (1999) do) so these findings are not representative of the population or generalizable across all disorders. There is a gap in knowledge about what is driving the gendered nature of COD and by looking at how childhood experiences are associated with COD differently by gender I provide essential knowledge about COD for males and females.

One theory that exists to explain the gendered variation in disorders focuses on the ways that males and females process negative emotions. For males, negative emotions are thought to be externalized, taking the form of aggressive or impulsive behavior, sometimes leading to personality disorders, conduct disorders, and SUD (Zahn-Waxler et al., 2008). For females, these negative emotions are thought to be internalized in the form of decreased social interaction, and can lead to mood disorders and eating disorders, but less often to SUD (Gjerde et al., 1988; Leadbeater et al., 1999).

Some hypothesize that the gendered variation observable in disorders is partially derivative of traditional sex-role traits and stereotypes. On one hand, as Zhan-Waxler and colleagues describe, the stereotypic adult female is nurturant, dependent, emotional, passive, and self-sacrificing (Zahn-Waxler et al., 2006), while on the other hand, the stereotypic adult male is aggressive, independent, and self-enhancing (Zahn-Waxler et al., 2006). Male-preponderant and female-preponderant disorders may then be reflective of the extremes of normative characteristics of boys and girls (Zahn-Waxler et al., 2006) as they cope with and express their negative emotions within the confines existing social norms and traditional gendered behaviors. This theory is an over-simplification of the gendered origins of psychiatric disorders and SUD; however, it offers insight into the influence of social norms in dictating disordered behavior. Existing theories have not extended this knowledge of gendered differences in disorder types to

theoretically explain how and why co-occurrence of disorders varies by gender. The research conducted for this dissertation will deliberately test gendered differences in the childhood social and material factors that affect disorder outcomes, and add to the dearth of knowledge in this area.

For females who have SUD, it is very likely that they also have a psychiatric disorder (Brady & Randall, 1999; Greenfield et al., 2007; Tuchman, 2010), while for males, SUD more often occurs in the absence of psychiatric disorder (Eaton et al., 2012). In contrast, females who have psychiatric disorder more commonly experience it in the absence of SUD. For males, psychiatric disorder is more often than not accompanied by an SUD.

The gendered prevalence patterns in individual disorders have been well-established using large, population-based datasets (Kessler et al., 2005). The gendered patterns in COD prevalence are less clear due to a lack of recent, population-based studies that are generalizable to the population, and the reliance on clinical samples for descriptions of gender differences (Najt et al., 2011). In addition to gendered patterns in types of disorders people develop, there are other variations in the experience of COD for males and females. Although COD is more likely to be present in males overall, when it is present for females, it has been described as more severe than it is for males (Korsgaard et al., 2016). This is an interesting finding, but the study it is based on was conducted with adolescents who had psychosis and SUD, limiting the generalizability of these results. Females are more likely to seek help than males when they have COD (Wu et al., 1999), although it is unclear if this is because of disorder severity, because of increased likelihood to access to healthcare services generally, or for a different reason altogether. It is possible that the order and timing of the disorders that comprise COD differ by gender, and for different types of disorders (e.g., mood disorders, personality disorders), though

these possibilities have not been investigated. This body of research suggests that there are theoretical gender differences underlying the pathway to COD, but more conclusive studies that are representative of the population are required to specify how risk factors affect men and women uniquely and how resulting experiences of COD differ by gender. Therefore, research that is focused on gendered differences in the antecedents of COD is essential.

1.3.3 Racial/Ethnic Differences in Co-occurring Disorder

Racial/ethnic differences in psychiatric disorder and SUD are pronounced: Hispanics as well as non-Hispanic Blacks have lower risk for internalizing disorders such as depression, generalized anxiety disorder, and social phobia compared to non-Hispanic Whites (Breslau et al., 2006). In addition, Hispanics have lower risk for dysthymia, oppositional-defiant disorder, and attention deficit hyperactivity disorder compared to non-Hispanic Whites, while non-Hispanic Blacks have lower risk for panic disorder, and early-onset impulse control disorders compared to non-Hispanic Whites (Breslau et al., 2006). Asian Americans have lower rates of all mental disorders compared to non-Hispanic Whites and other racial/ethnic groups (Breslau et al., 2005). Also, lower risk of psychiatric disorder among minorities is more pronounced at lower levels of education (Breslau et al., 2005), potentially indicating a conditional relationship between socio-economic status and race/ethnicity in psychiatric disorder outcomes. Racial/ethnic differences again appear in SUD: both Hispanics and non-Hispanic Blacks have an equivalent or lower rate of disorder; however, their disorders can be more persistent despite treatment (Grant et al., 2012) and may last longer overall (Arndt et al., 2010) than non-Hispanic Whites. Hispanics also have lower rates of COD than non-Hispanic Whites do (Vega et al., 2009). Asian Americans have dramatically lower rates of SUD than other racial/ethnic groups (SAMSHA, 2012).

The abuse of substances is less common in Asian American, Black, and Hispanic racial/ethnic groups than it is for non-Hispanic Whites, and as such, when it occurs, it may be associated with more stress and social isolation (Hwang et al., 2008). Both Hispanic and non-Hispanic Asian American women face more rigid cultural sanctions against alcohol use than do their non-Hispanic Black and non-Hispanic White female counterparts (Keyes et al., 2011; Mulia et al., 2009), which may explain their lower rates of disorder relative to non-Hispanic Whites. Most of this research on racial/ethnic differences in disorder is limited to just psychiatric disorder, or just SUD: little conclusive knowledge about the racial/ethnic differences in COD has been established. This dissertation, in addition to establishing rates of COD relative to psychiatric disorder only, SUD only, and no disorder by racial/ethnic group will also test for racial/ethnic differences in the social factors that put people at risk of developing COD: an understudied phenomenon.

Increased exposure to discrimination and stressors that are unique to racial/ethnic minorities typically produces health outcomes that are worse for racial/ethnic minorities than for non-Hispanic Whites (Paradies et al., 2015; Williams, 1999). Consequently, poorer mental health and substance use outcomes might be expected for non-Hispanic Blacks, Hispanics, and Asian Americans than non-Hispanic Whites. Interestingly, this is not the case though the mechanisms underlying this paradox are not well understood. Social stigma and social consequences that apply especially to minority women and specifically to SUD may play a part, along with specific mechanisms related to differences in coping strategies and resources between racial/ethnic groups (Hwang et al., 2008).

Hispanics report stronger family ties than those in other racial/ethnic groups (Hummer & Hamilton, 2010) and, in turn, are more likely to rely on familial social support networks for

coping with stress than other racial/ethnic groups (Hwang et al., 2008). This use of familial support is associated with adaptive coping styles that can ameliorate the stressors that cause mental health and substance use problems and may replace other avoidant/escape coping styles (Moos, 2007). The direct testing of a familial support advantage for the Hispanic population with respect to COD was not found in the review of literature for this dissertation, but would help to ascertain the role of this beneficial resource for Hispanics.

Prevalence rates among Asian Americans may be low in particular because of childrearing practices that support adaptive coping, extended family structures that provide multiple tiers of support, access to cultural and community resources, and a higher tendency toward spirituality that encourages resilience (Sue et al., 2012), although the precise reasons for low levels of psychiatric disorder in this population are not certain. Authors have noted that psychiatric disorders are culturally defined and may be both expressed and experienced differently by Asian American subgroups than they are for Whites (Lam et al., 2004; Okazaki, 2002; Watters, 2010). This may also be true for the Hispanic population. Careful attention should be paid, then, to the role of acculturation, immigration, and experiences with microaggression in understanding CODs for Asian Americans and Hispanics, as well as other immigrant groups (Lam et al., 2004; Okazaki, 2002; Watters, 2010).

For Non-Hispanic Blacks, stress relief through overconsumption of "comfort foods" high in fat and calories has been proposed as a theory to explain why the effects of stress among non-Hispanic Blacks more commonly manifest as physical health problems than as psychiatric disorders or SUD (Jackson et al., 2010). Social support for non-Hispanic Blacks typically comes from extended networks rather than from immediate family, from friends, and through participation in religious institutions (SAMHSA, 2001). Religious coping, common for non-

Hispanic Blacks, reduces the risk for disorders, and may contribute to lower disorder rates for non-Hispanic Blacks compared to non-Hispanic Whites: a hypothesis that has been proposed but not been confirmed (Hamilton et al., 2013; Staton-Tindall, 2013).

For the most part, with the exception of the study by Vega and colleagues (2009) looking at dual diagnosis in Hispanics, the literature presented above is restricted to only one kind of disorder, *either* psychiatric disorder *or* SUD: little definitive evidence exists to describe and explain the racial/ethnic differences in COD, and this study enables a fuller understanding of these phenomena. Further, the theories proposed above require more testing to solidify their role in explaining mental health and substance use differences for racial/ethnic groups. To date, no studies have been found that look at combined racial/ethnic and gender differences in COD, although the need for intersectional research on COD that studies multiple social statuses in tandem, and not as the sum of their parts, is clear (Bauer et al., 2014).

The lack of research on the social origins of racial/ethnic and gender differences in COD is due to the problems described in this presentation of the literature: disorder-specific research, the tendency for COD research to be restricted to non-representative clinical samples, and the focus on genetic and biological determinants of COD. By looking at variations in COD in a large, representative sample, as I do in this dissertation, I am able to respond to these weaknesses and analyze the relevance of social factors to disorder outcomes by race/ethnicity and gender. This represents an important contribution brought to the field by this dissertation: it clearly establishes trends in antecedents for COD for racial/ethnic groups and for males and females, at the population level.

1.3.4 Childhood Poverty and Co-occurring Disorder

Now turning from variations in substance use and psychiatric disorder prevalence to look at some of the factors that contribute to the development of COD, the literature has found childhood poverty to be an important determining factor. This study considers childhood poverty to be separate from other childhood adversities, which will be detailed below. Exposure to childhood poverty increases experiences of other stressors during childhood, but is not itself considered a stressor (Evans, 2004). Exposure to poverty or to economic adversity in childhood has been linked to increased odds of experiencing psychiatric disorder (Costello et al., 2003), disordered substance use (Buu et al., 2009; Ensminger, Joun, & Fothergill, 2002; Najman et al., 2010), and the co-occurrence of both types of disorder (Banducci et al., 2014) when compared to those with no such exposure.

The impact that childhood poverty has on mental health may operate at least partially through increased exposure to other childhood adversities such as abuse, harmful substance use in the household, parental psychiatric disorder or suicidality, and low levels of parental warmth (Menard, Bandeen-Roche & Chilcoat, 2004) although the authors of the study do not test this specifically. Poverty in childhood may also hinder access to resources that can ameliorate stressors such as parental support, positive peer networks, mentorship, and so on, allowing stressors to impact psychiatric outcomes (Umberson, 2014).

The Theory of Fundamental Causes sees variation in health conditions by socio-economic position (SEP) as a result of ability to access resources. This theory can be used to explain why the relationship between experiencing childhood poverty early in life and COD may be inherently tied to race and gender, as I hypothesize in this study. The Theory of Fundamental Causes suggests that people with high SEP have a host of flexible resources (knowledge, money,

power, prestige, and beneficial social connections) that they can source to mitigate a range of risks and to access a range of protective factors, resulting in a health advantage for high SEP individuals. Individuals growing up in poverty are likely to experience a cluster of disadvantage throughout the life course (DeNavas-Walt et al., 2015) and thus possess a continual diminished ability to access resources that could be protective against COD.

Using the Theory of Fundamental Causes in combination with the literature reviewed for this dissertation, a logical hypothesis would be that childhood poverty will be more strongly associated with COD for racial/ethnic minorities than for non-Hispanic Whites primarily because non-Hispanic Whites (who are accorded more resources –not just economic— due to their social status) can use the resources they have (i.e. access to environments that promote healthy mental well-being, health insurance to cover expenses when they seek treatment for a disorder, etc.) to create healthy situations for themselves that reduce the risk of COD. This remains untested in the literature I reviewed for this study. Similarly, women often have fewer opportunities for economic advancement throughout their lives than men, and I suspect they are more impacted by childhood poverty than men due to the relatively fewer flexible resources they have available to promote their own mental health.

It is unknown whether the impact of exposure to poverty in childhood on COD varies both by gender and by race/ethnicity. By providing an analysis of this critical relationship by gender and race/ethnicity, this study is poised to address and assuage the current uncertainty regarding childhood poverty and COD, its variance for males and females, and for different racial/ethnic groups. My dissertation is able to make this key contribution because of its large sample size and its generalizability to the population. It has the ability to detect differences that

exist and a theoretical frame that brings much-needed attention to the intersections of social status and childhood experiences.

1.3.5 Childhood Adversity and Co-Occurring Disorder

Significant recent interest in childhood adversity and its relationship to adult health outcomes has led to the inclusion of childhood adversity in many large, national studies (Afifi et al., 2011; Dube et al., 2003; Keyes et al., 2011). National data show that 58.3% of adolescents report at least one adversity and, of this group, 59.7% report multiple adversities (McLaughlin et al., 2012). Childhood stressors or adversities include experiences such as: physical abuse, sexual abuse, emotional abuse, parental psychiatric disorder, parental or family SUD, family structure changes (including loss), parental imprisonment, witnessing abuse/violence, and life threatening events. These adverse childhood experiences are associated with SUD (Kessler et al., 1997; Dube et al., 2006; Felitti et al., 1998; Pilowsky & Wu, 2006), a host of psychiatric disorders (Cohen, Brown & Smaile, 2001; Edwards et al., 2003; Green et al., 2010; Kessler et al., 1997; Mullen et al., 1996), and COD (Banducci et al., 2014).

Research from the Adverse Childhood Experiences Study has shown dose-response type relationships between stressors during childhood and mental health and substance use outcomes later in life (Dube et al., 2003; Chapman et al., 2004; Anda et al., 2002). The population-attributable risk proportion is 28.2% for adversity and onset of any psychiatric disorder (McLaughlin et al., 2012). Previous research with the NESARC I and II datasets confirm that childhood adversities are highly prevalent and highly correlated with psychiatric disorder in the population (Cavanaugh et al., 2015) as well as substance use disorder (Evans and Upchurch, 2016).

A few studies have examined the heterogeneity inherent in childhood stressors, in terms of types of adversity and the severity of exposure, with findings revealing distinct clusters of adversity that are associated with different degrees of psychopathology (Menard, Bandeen-Roche & Chilcoat, 2004; Dunn et al., 2011). Stressful childhood experiences related to maladaptive family functioning tend to cluster in the population, including: parental psychiatric disorder, SUD, and criminality; family violence; physical abuse; sexual abuse, and neglect. These family functioning experiences correlate the most strongly with onset of disorder relative to other adversities in childhood, such as parental divorce or loss (McLaughlin et al., 2012).

The influence of childhood adversity on COD can be understood through a stress-coping model of psychiatric disorder and addiction. Growing up exposed to multiple childhood adversities often also indicates being in an environment where there are few positive examples of healthy, adaptive coping but many exposures to negative events and circumstances. The exposure to negative events increases risk for COD by elevating stress, inhibiting even minimal support or reinforcement for healthy coping and adaptation from the social network, and ultimately, decreasing ability to withstand mental hardship while simultaneously increasing desire to cope through excessive substance use (Wills & Hirky, 1996). Exposure to stressors in childhood also leads to neurobiological sensitivity to stress that increases vulnerability to developing psychiatric disorders (Heim et al., 2010). Likely, multiple pathways are operating in the way that childhood adversities affect mental health, but this is not something tested routinely or systematically in the literature reviewed here.

Since childhood adversities tend to co-occur, it is important to study the potential heterogeneity of stressful experiences or clusters of experiences because different types may be associated with different probabilities of disorders or their timing. Providing effect estimates for

an individual stressor can be misleading because doing so can misattribute the effect of differing or multiple stressors to the single stressor under study, thus biasing the effect estimate. The impact of multiple adverse events has been established to be stronger than the effect of a single adverse event for mental health outcomes, and may occur in a non-linear relationship (Anderson et al., 2002; Kessler, Davis, & Kendler, 1997). Current studies of adversity do not properly account for the compounding nature of stressors, despite suggestions this relationship exists and that stressors may amplify each other (Anderson et al., 2002). Furthermore, a summative score can mask important information about the impact of different types of events and a categorization based on adversity type can result in varying strengths of association with mental health outcomes (Turner, Finkelhor, & Ormrod, 2006; Turner & Lloyd, 2003).

The historical failure to properly account for lifetime adversity has resulted in the systematic underestimation of the role of stress exposure in psychiatric disorder (Turner Wheaton, & Lloyd, 1995). This underestimation can be corrected by looking at the conditional nature of childhood stressors with respect to each other and in light of experiencing childhood poverty, both important in estimating their associations with COD, as I do here. A methodological advance presented by this study is the critical investigation done to determine the optimal operationalization of childhood adversity for COD research. I present researchers in the field with measures developed specifically with the purpose of capturing variation in COD due to adverse experiences, and I do so based on the findings of extensive analyses.

1.3.6 Differential Impact of Childhood Stressors by Gender and Race/Ethnicity

Adversities in childhood, much like psychiatric disorder and SUD, are gendered and racialized experiences, even occurring at different rates depending on race/ethnicity and gender. In addition to this, literature suggests that these adversities have varying strengths of association

with psychiatric disorder by race/ethnicity and gender (Muenzenmaier et al., 2014; Duhig et al., 2015), and SUD (Ali et al., 2016). Thus, it is also plausible that the relationship between childhood adversity and COD differs by race/ethnicity and gender: and I test this possibility in this study.

Childhood stressors are tied to family structure and experiences, and include (as mentioned above), parental psychiatric disorder, SUD, and criminality; family violence; physical abuse; sexual abuse, and neglect. A study on mothers and fathers with COD (Ali et al., 2016) found that when mothers have COD, there is a stronger correlation with their adolescent children exhibiting SUD, than when fathers have COD (Ali et al., 2016). Additionally, mothers' COD may be more impactful for their daughters than their sons in terms of likelihood of SUD in the children (Ali et al., 2016). Child sexual abuse is more strongly associated with psychiatric disorder for females than males, while parental incarceration is more strongly associated with psychiatric disorder for males than females (Rosenberg et al., 2007; Muenzenmaier et al., 2014). Exposure to childhood trauma, generally, is correlated with psychosis, depression, and anxiety more strongly for females than males (Duhig et al., 2015). Thus, it is apparent that gender differences in the connection between types of adversity and psychiatric disorder and SUD have been demonstrated in existing literature, but the findings require further confirmation for these trends to be solidified, and extended from single disorder types to COD.

The connection between childhood stressors, childhood poverty, and negative mental health and SUD outcomes may be not the same for all racial/ethnic groups (Rosenfield, 2012). However, the presence of a conditional relationship between childhood adversity and race/ethnicity for the development of COD was not tested in the literature reviewed for this dissertation. Whether these differential associations exist is at present unclear, primarily due to

the fact that both racial differences in COD and antecedents of COD have been dramatically understudied (Brown et al., 2013; Rosenfield and Mouzon, 2013). These phenomena must be tested and reported–something I do in this dissertation.

In prior research, specific childhood adversities have been studied, but in isolation from others, limiting generalizability. Existing work in this area, however, does point to gender differences in the relationship between childhood adversities and substance use and psychiatric disorders separately (Fisher, et al. 2009), but does not look at the impact of childhood stressors on disorders occurring together. Little consensus about race/ethnicity and gender differences in effects of adversities exists amongst these studies, a feature most likely attributable to different samples, measurement strategies, and definitions of disorder. Based on studies that show that the impact of different childhood adversities on psychiatric disorder and SUD operates differently by race and gender, there is reason to believe the impact of childhood stressors on COD is not universal (Curran et al., 2016). With a sample size sufficient to study these intersecting social factors, I undertake an investigation of COD that breaks through the historically siloed fields of mental health and addiction research and bring clarity to the relationships between the childhood social environment and co-occurring psychiatric disorder and SUD that are often treated as unrelated.

1.3.7 Early Onset and Timing of Disorders

In addition to understanding the social factors that affect the development of COD, it is also important to study how timing factors into the onset of disorders, and how co-occurrence is affected by the order of disorder onset within COD. While many pathways to COD are possible, the most typical pattern involves a psychiatric disorder preceding SUD by 5-10 years (Kessler, 2004), a finding based on bivariate age of onset data from the National Comorbidity Survey

conducted in the early 1990's. While others have replicated this finding with more complete multivariate models in more recent population-based data (Martins et al., 2009), they have limited their investigations to multiple psychiatric disorders with a single SUD (Martins et al., 2009), multiple SUDs with a single psychiatric disorder (Breslau et al., 2003), or have looked only at SUD following psychiatric disorder (Swendsen et al., 2010) rather than the possibility of the reverse order of COD onset. It is, therefore, important to establish the trends in onset of COD using all psychiatric and all alcohol and drug use disorders in a recent, population-based dataset.

Other studies on both alcohol and SUD in clinical samples have confirmed that there is a tendency for psychiatric disorder to occur first overall (Najt et al., 2011). When there is early onset of the first psychiatric disorder, especially in the cases of early onset depression and early onset bipolar disorder, the second disorder (usually SUD) is likely to have an earlier onset than it does when SUD is not preceded by another disorder (Winokur et al., 1996; Grant et al., 1996). Should the less-typical pattern occur, and SUD precedes psychiatric disorder, the severity of the COD tends to be lessened and treatment outcomes are improved compared to COD with psychiatric disorder first (Najt et al., 2011).

Limited work has been conducted to test relationships between poverty and stressful events in childhood and the timing of onset of psychiatric disorder and SUD. Nonetheless, physical and sexual abuse appear to shorten time to onset of psychiatric disorders (Brown et al., 2005; Garno et al., 2005; Leverich et al., 2002) and emerging research extends this finding to verbal abuse as well (Post et al., 2015). Additionally, a small body of work suggests that cumulative exposure to adverse events increases risk of early onset psychiatric disorder and substance use separately (Green et al., 2010; McLaughlin et al., 2012).

Events occurring before puberty (a critical period, or limited window during which an exposure or event can have adverse or protective effects on subsequent outcome) can influence the development of COD in dramatic ways, therefore it is important to include critical periods along with a Life Course Perspective when considering possible timings of disorder (Umberson et al., 2014). Events that have been found to be impactful when they occur in a critical period include: parental divorce, physical abuse, and sexual abuse (Ross & Mirowsky, 1999). Investigators have also reported that the combination of severe childhood stressors with recent life stress multiplicatively increases the likelihood of psychiatric symptoms and disorders, suggesting that early and severe stress may create a lifelong non-linear vulnerability to stress (George, 2007). These findings underscore the importance of examining how the occurrence of childhood poverty and stressors affects the timing of COD development, as well as a temporal approach.

I bring the Life Course Perspective into this study deliberately to frame my understanding of how the lives of family members are inextricably linked and how events in early life stages can set the course for later psychiatric outcomes. This adds a new perspective to COD research: emphasizing social factors (over genetic influences) and introducing an intentional and theoretical temporality to a largely atheoretical field of work.

1.3.8 Other Factors Influencing Co-Occurring Disorder

Parental psychiatric disorder and SUD can create inconsistent and disruptive home environments and parenting due to variation in parental availability, attentiveness, and behavior. However, both may play another role in the development of COD. Parental and other familial disorder –controlling for the inevitably stressful experiences this disorder generates in home environments— may also provide an indication of some of the genetic transmission of risk for

developing psychiatric disorders. Parental SUD specifically may additionally indicate role modeling of unhealthy relationships with substances or unhealthy coping strategies (DiClemente et al., 2001).

Strong social support can ameliorate the negative impact of stressors and can be protective against the development of psychiatric disorder and SUD. Support can occur in the form of familial support, friend group support (when the friends are positive rather than negative influences on coping mechanisms), mentorship or elder support, and religious or faith-based support (Rhodes et al., 2005; Milot et al., 2009; Allen et al., 2003).

Studies done within a Stress Process Model frame have shown that the deleterious psychological impacts of stressors can also be mitigated by sense of control/mastery, self-esteem, emotional reliance, assertion of autonomy, and mattering (Thoits, 2010; Wheaton, 1980; Pearlin et al, 2005). In particular, Turner and Butler hypothesize that childhood trauma impacts later mental health outcomes by changing support structures, reducing integration into networks, and increasing social isolation. In their study, they find that low levels of support have direct effects on well-being and can increase the deleterious impact of stress (Turner & Butler, 2003).

1.3.9 Limitations of Existing Co-occurring Disorder Research

Unfortunately, past research on COD has been affected by several severe problems: 1) inconsistent definitions used for COD; 2) a narrow focus on single disorders or single substances; 3) a predominance of research conducted on clinical samples; 3) a primary focus on treatment outcomes rather than prevention, and 4) a tendency to not account for potential racial/ethnic and gender differences in antecedents of COD.

The lack of a standardized definition for COD has resulted in inconsistent research and treatment (Buckstein et al., 1989), with individual providers and researchers fashioning

definitions specific to their clinical populations (Todd et al., 2004). Examples of different definitions used in existing research include: *"the co-existence of a psychoactive chemical use disorder with another major psychiatric disorder,"* a definition that does not specify SUD criteria or psychiatric disorder criteria and excludes non-psychoactive substance use as well as psychiatric disorder that are not "major," this definition also requires the disorders to overlap temporally (Sheehan, 1993). Another definition used in the literature is, *"one of three mental disorder categories, namely personality disorder, mental illness and intellectual disability with intoxication, harmful substance use, or dependence"* (Soothill et al., 2012). This definition is broad, indicating that any intoxication even if it is not in the context of an SUD can be enough to categorize someone as having dual diagnosis, if they have an existing mental disorder, and does not specify the time period that should be used for operationalizing the definition. Generally, definitions of COD lack clarity regarding what time span to use for assessment, which leaves open questions about how close to one another the disorders must occur for an individual to have COD. Few established definitions of COD include the possibility of diagnosis changing over time, or if an individual can ever be in "recovery" from COD.

Most studies have used inconsistent or poorly defined comparison groups: sometimes comparing outcomes for people who have COD to people who just have SUD (e.g., Bartels et al., 1995), sometimes comparing outcomes for people who have COD to those who just have psychiatric disorder (e.g., Mueller et al., 1994), sometimes comparing outcomes for people who have COD to those who have no disorder (e.g., Breslau et al., 2003) and sometimes using combinations of these comparison groups in the same study (Grant et al., 1996). Since each of these comparison groups is different, they produce incomparable findings with respect to the

impact of COD and as a result it is difficult to generalize across the limited COD studies that exist.

Most COD research is disorder- and substance-specific (e.g., a study of people with co-occurring schizophrenia and marijuana use disorder). This type of segregation by substance type and psychiatric disorder type becomes problematic in the study of COD for three reasons: first, to do so is inconsistent with the conceptualization of substance use problems existing on a continuum (as in *DSM-5*) that, for example, may begin with alcohol abuse and over time come to involve the abuse of another or multiple substances; secondly, different disorders likely stem from causes that are more similar to each other than they are different (West, 2006), and third, the act of restricting analyses by substance and disorder limits the generalizability, sample size, and statistical power necessary to examine COD. Additionally, research on COD has primarily been conducted in non-random convenience samples of patients enrolled in treatment programs, limiting generalizability to the general population.

Most COD research remains focused on its treatment, rather than on its determinants. Researchers have extensively studied the high lifetime prevalence (up to 50% in the population of people with an existing disorder), age of onset for COD (Kessler et al., 2005), and the relatively poorer treatment outcomes (Najt et al., 2011), yet hardly any work has concentrated on the antecedents of COD. A related lacuna in current knowledge is that most COD research, as with most SUD research (Lettieri et al., 1980; West, 2006), is conducted within an atheoretical framework (West, 2006). My dissertation study substantiates the guiding theoretical framework I propose for this research and introduces theoretically-grounded findings about COD to a field plagued by atheoretical research.

Gender differences in the factors that shape COD have been overlooked, despite evidence that women and men commonly develop different types of disorders (Kessler et al., 2005). Racial/ethnic differences in COD have also been understudied, though it is apparent that racial/ethnic differences in prevalence of COD exist (Kessler et al., 2005). Stressors are inversely associated with most disorders; yet, non-Hispanic Blacks have lower rates of most disorders than non-Hispanic Whites while having higher exposure to stressful events and circumstances. Moreover, these social statuses may intersect to produce complex disparities in COD, a possibility that has been ignored in existing research on COD. The conjunction of these problems in COD research calls for a population-based study that examines antecedents of COD and their variance by race/ethnicity and gender in a study sufficiently powered to detect these differences. I deliver this critical contribution here, in this dissertation.

1.4 Innovative Contribution of the Dissertation

This study provides answers to many of the current uncertainties described above, including the following: what relationship may exist between childhood poverty and COD for males and females, and for different racial/ethnic groups; the differential impact of childhood adversities on COD for various racial/ethnic groups; the differential impact of childhood adversities on COD for males and females; and how the occurrence of adversities affects the timing of COD development by gender and by race/ethnicity. This type of testing for conditional relationships is critically lacking in existing COD literature and as a result there is a risk of misunderstanding the relationship between childhood experiences and resulting psychiatric and SUD.

In addition, I provide several key innovations that move this field of inquiry forward. I use a theory-based approach to guide the study of the association between early social factors and COD. This use of theory is rare in research on co-occurring substance use and psychiatric disorders but adds considerable depth to the investigation and understanding of the phenomenon and aids in interpretation of findings: in this case allowing them to be situated within the theoretical understanding of how childhood poverty and adversity are related to the development of disorders. My focus on social factors associated with development of COD rather than biological or genetic risk is important. Many studies highlight the genetic components of disorder development, and by instead turning the focus to the childhood social and material environment, I bring the spotlight to an understudied area of COD research and one that is modifiable.

This dissertation uses a time-dependent measure of COD (age of onset) to investigate how stressors influence timing of COD: something completely missing from current COD research. Testing different operationalizations of childhood adversities allows this study to be responsive to the suggestion that stressors may accumulate and influence each other in a more complicated manner than simply as an additive sum.

This study considers multiple substance and psychiatric disorders together, to show patterns that exist in COD development across disorders, without restricting the sample to disorder- or substance-specific outcomes. In doing so, I study the full process of COD development, and provide information that is generalizable to multiple disorders. This dissertation helps to bridge the divide between research in the two related fields of mental health and addiction that typically research outcomes in silos.

I do all of this using a large, recently collected, nationally-representative survey dataset with sample weights allows the conclusions to be generalized to the US population and increases the external validity of the findings: a clear strength of this study.

In summary, this research advances the scientific literature on COD by providing information on the connections between poverty and stressors in childhood and their linkage to COD for males and females and for different racial/ethnic groups. This is the first study to my knowledge to present research on race/ethnicity and gender differences in the early social factors that affect COD with sufficient sample size to properly test associations. Further, the survival analysis used in this dissertation tests the timing of disorder onset and how disorder sequence may matter differently by gender and by race/ethnicity: an assumption previously untested in this body of work.

1.5 Chapter Summary

Chapter 1 introduced the study undertaken in this dissertation. I summarized existing research on COD showing clear gaps in the understanding of experiences of COD for different demographic groups in the population despite knowledge of how psychiatric disorders and SUD vary in prevalence for males vs. females and for Whites compared to Blacks, Hispanics, and Asian Americans. I argued that existing COD research does not properly estimate the effect of childhood poverty and childhood adversity on disorder outcomes, and that the lack of investigation of differences by gender and race/ethnicity is problematic. Finally, I described the key contributions that my study will make to the body of knowledge on COD: including the introduction of a theoretical perspective, the examination of gender and race/ethnicity differences, and the use of a sample that is representative of the US population, among others.

CHAPTER 2: RESEARCH QUESTIONS & THEORETICAL APPROACH

Chapter 2 presents the research questions that are examined in this study organized into three overarching Aims. This chapter also presents corresponding hypotheses for each of the questions under study. I then describe the conceptual model used and provide a description of the three theories used to develop the conceptual model that guides the dissertation research. I conclude by explaining the theoretical reasons for expecting differences in the relationships under consideration by race/ethnicity and gender.

2.1 Contribution to the Literature

In summary, there is a paucity of literature on the impact of childhood poverty and childhood stressors on COD in general, and almost no studies have been found that look at differences for racial/ethnic groups or for males and females. The potential conditional processes operating in these relationships are currently unknown and the lack of certainty in these areas leaves significant risk of assuming the dominant pathways and relationships exist for all racial/ethnic subgroups and for males and females universally. There is substantial existing evidence suggesting psychiatric disorder and SUD vary by race/ethnicity and gender, and I expect the antecedents do not behave universally, though they are currently treated that way. Thus, this dissertation study adds considerably to the body of scientific knowledge in this area and significantly advances the understanding of racial/ethnic and gender differences in COD.

2.2 Overall Goal and Approach

The overall goal of this study is to better understand the role of childhood poverty and childhood adversity in the occurrence of COD for males and females, and for different

racial/ethnic groups, and to assess whether or not poverty and childhood adversity render the same effect on timing of occurrence of psychiatric disorders and SUD for all racial/ethnic groups and for males and females.

Using the elaboration model (Aneshensel, 2013; Rosenberg, 1968), this study establishes whether the focal relationship between childhood poverty and COD is present when alternative explanations and confounders are considered. This dissertation also tests whether various types of childhood stressors explain or intensify the relationship between childhood poverty and COD for males and females and for different racial/ethnic groups.

2.3 Research Aims

2.3.1 Aim 1

Aim 1: To determine if there is an association between childhood poverty, childhood stressors, and COD lifetime occurrence. The research questions addressed in this Aim are:

a) Are childhood poverty and childhood adversities (count of childhood stressors, frequency of sexual abuse, frequency of physical/verbal abuse) associated with lifetime occurrence of COD?
b) To what extent does this association differ by racial/ethnic group?
c) To what extent does this association differ by gender?

Related Hypotheses:

- Hypothesis 1a1: The experience of poverty in childhood will be positively associated with lifetime occurrence of COD.
- Hypothesis 1a2: Childhood stressors will be associated with lifetime occurrence of COD and will partially explain the association of childhood poverty and COD.

- Hypothesis 1b1: Different types of childhood stressors (count of childhood stressors, frequency of sexual abuse, frequency of physical/verbal abuse) will affect COD differently by racial/ethnic group, with frequency of sexual abuse and frequency of physical/verbal abuse being more strongly associated with COD in non-Hispanic Whites compared to all other racial/ethnic groups.
- Hypothesis 1b2: Childhood poverty will affect COD differently by racial/ethnic group, with childhood poverty being more strongly associated with COD in non-Hispanic Whites compared to all other racial/ethnic groups.
- Hypothesis 1c1: Different types of childhood stressors (count of childhood stressors, frequency of sexual abuse, frequency of physical/verbal abuse) will affect COD to varying degrees based on gender, with sexual abuse frequency more strongly associated with COD in females than males.
- Hypothesis 1c2: Childhood poverty will be more strongly associated with COD in males than females, and with males this association will be stronger relative to psychiatric disorder only than to SUD only.

2.3.2 Aim 2

Aim 2: To determine if the effect of childhood poverty on lifetime COD is intensified by the experience of childhood stressors. The research questions addressed in this Aim are:

a) Is the impact of childhood poverty on the likelihood of developing COD over the life course intensified by childhood stressors (count of childhood stressors, frequency of sexual abuse, frequency of physical/verbal abuse)?
b) To what extent do any conditional relationships differ by racial/ethnic group?
c) To what extent do any conditional relationships differ by gender?

Related Hypotheses:

- Hypothesis 2a: Poverty in childhood will be more strongly associated with COD among people who have experienced more childhood stressors relative to those who have experienced fewer stressors.
- Hypothesis 2b1: The count of childhood stressors will intensify the association between childhood poverty and COD relative to psychiatric disorder only and SUD only for all racial/ethnic groups.
- Hypothesis 2b2: The magnitude of these associations will differ by race/ethnicity.
- Hypothesis 2b3: The specific types of childhood stressors that intensify the effect of poverty will differ by race/ethnicity.
- Hypothesis 2c1: The count of childhood stressors will intensify the association between childhood poverty and COD for both males and females.
- Hypothesis 2c2: The magnitude of these associations will differ by gender.
- Hypothesis 2c3: The specific types of childhood stressors that intensify the effect of poverty will differ by gender.

2.3.3 Aim 3

Aim 3: The third Aim of this dissertation is to estimate the association between having experienced poverty and different types of stress in childhood and the timing of developing lifetime COD among those who have COD. The research questions addressed in this Aim are:

a) How does experiencing childhood poverty affect hazard of COD onset over time?
b) Are some types of childhood stressors associated with COD onset over time more strongly than others, or more strongly than no stressors?
c) What is the hazard of co-occurrence once one develops a psychiatric disorder?

d) What is the hazard of co-occurrence once one develops SUD?

e) To what extent does this risk differ by racial/ethnic group?

f) To what extent does this risk differ by gender?

Related Hypotheses:

- Hypothesis 3a: Childhood poverty will be associated with an increased risk of COD over the life course.
- Hypothesis 3b: Childhood stressors will be associated with increased risk of COD over the life course. Sexual abuse will add additional risk to the risk incurred by all other stressors.
- Hypothesis 3c: The rate of co-occurrence for those who have a psychiatric disorder first will be greater than for those who experienced SUD first.
- Hypothesis 3d: The hazard of co-occurrence for those who have a psychiatric disorder first will be greater for those who experienced childhood poverty than those who did not.
- Hypothesis 3e: The hazard of co-occurrence for those who have SUD first will be greater for those who experienced childhood stressors than those who did not.
- Hypothesis 3f: Risk of co-occurrence for males will be higher than females in both those with SUD first and those who experience psychiatric disorder.
- Hypothesis 3g: Risk of co-occurrence for non-Hispanic Whites will be higher than all other racial/ethnic groups in both those with SUD, and those with psychiatric disorder.

2.4 Theoretical Framework

For this study, I draw heavily on the Stress Process Model (Pearlin et al., 1981) and bring in concepts from the Life Course Perspective (Elder, 2003) with an understanding of the antecedents of disorder from the Theory of Fundamental Causes (Link & Phelan, 1995). Together these three theoretical perspectives shape my understanding of the interplay between social environments, stress, and psychiatric health outcomes throughout peoples' lives. The integration of these theories has led to the development of a conceptual model with specific associations that are tested in this dissertation. After describing the Stress Process Model, the Life Course Perspective, and the Theory of Fundamental Causes, I will then explain how they combine in the comprehensive model to guide the dissertation.

2.5 Theories Used in the Dissertation

2.5.1 The Stress Process Model

Researchers have comprehensively demonstrated links between social environment and psychological well-being (Umberson et al., 2014). Much of this demonstrated relationship between social environments and psychiatric disorder has been explained through the Stress Process Model (Thoits, 2010) which hypothesizes that disorder develops according to differing exposures to social and environmental stresses and differing access to ameliorative resources. The Stress Process Model appears extensively in the literature as a tool for explaining the development of psychiatric disorder in individuals (Aneshensel & Mitchell, 2014). The Stress Process Model explains the way life events, chronic strains, self-concepts, coping, and social supports come together to form enduring processes of stress proliferation. Life events adversely affect role strains, and these exacerbated strains go on to erode positive concepts of self, seen

through diminished self-esteem and mastery (Pearlin et al., 1981). The lowered levels of self-concept then translate into vulnerability for experiencing symptoms of stress (Pearlin et al., 1981). Resources such as coping ability and the presence of social supports can mediate this process and prevent the translation of strain into poor mental health outcomes (Pearlin et al., 1981).

In a Stress Process Model framework, the experience of adverse events in childhood is believed to increase the likelihood of developing disorder through a variety of mediating variables (Turner & Butler, 2003). The conditions and social characteristics that predict stress exposure include socioeconomic position (SEP), family type, neighborhood disadvantage, and neighborhood integration/segregation. The resulting stressful exposures, characterized as eventful life stressors, chronic stress, and lifetime traumas (Thoits, 2010; Wheaton, 1980; Pearlin et al., 2005), can be mitigated by social support and social networks, sense of control/mastery, self-esteem, assertion of autonomy, and mattering (Thoits, 2010; Wheaton, 1980; Pearlin et al., 2005; Turner & Butler, 2003; Turner & Lloyd, 1995). The stress exposure and the beneficial resources work in tandem to produce outcomes of mental and physical health and/or disorder. Studies that have applied the Stress Process Model to psychiatric disorder have noted both the profound accumulation of risk factors and a corresponding lack of protective factors in individuals with the lowest SEP (Turner & Lloyd, 1999). Turner and Lloyd describe resulting higher rates of psychiatric disorder in the lowest SEP group (1999), making the Stress Process Model a natural fit with other theories addressing social stratification.

In particular, the part of the Stress Process Model that I draw on in this dissertation is the sociological study of stress, as articulated by Pearlin (1989). In harmony with the theory proposed by Pearlin, I highlight the important of race/ethnicity and gender as factors that

determine membership in status groups and correspondingly examine their role in the stress process. Pearlin (1989) notes that these statuses inherently control exposure to and meaning of stressors, access to mediators, and ultimately psychological and behavioral manifestations of stress. I incorporate these understandings in the way this dissertation uses constellations of stressors rather than particular stressful events and uses family support as a stress mitigation variable.

2.5.2 The Life Course Perspective

The Life Course Perspective is a theoretical approach that draws attention to pathways and patterns in the timing, length, spacing, and sequence of events, roles, and health and social outcomes (Elder, 2003). This theoretical framework is a multidisciplinary paradigm that guides the study of people's lives, structural contexts, and social change. In particular, the Life Course Perspective brings to the forefront of study the powerful connection between individual life trajectories and the unique historical and socioeconomic context in which these lives unfold. The theoretical perspective of the Life Course is based on five key principles: lifespan development, personal agency, linked lives, historical time and geographic place, and timing of decisions (Elder, 2003). The life course, in this theory, is understood to be, "a sequence of socially defined events and roles that the individual enacts over time" (Giele and Elder, 1998, p. 22).

The Life Course Perspective looks at age-differentiated social phenomena as the sum total of a person’s experience or as a sequence of transitions that are enacted over time, not as linear or discrete events but as continuous processes (Elder, 1985). Elder notes that individuals in a family have a shared history and interact within constantly changing social contexts across time and geographic space (2003). In this theoretical perspective, behavior and decisions do not occur in a vacuum because people and families interact with each other and within sociohistorical time.

Timing of transitions is important to study as atypical transitions can decrease the odds of success in a trajectory, such as early parenthood decreasing the likelihood of completing a high school education (Giele and Elder, 1998).

To respect the heterogeneity or diversity in life course processes, it is essential to consider not only average developmental trends, but also variation in individual experiences of development. The ability to adapt to changes over the life course may vary with the resources or supports inherent in economic or social capital (George, 2007). The Life Course Perspective recognizes increasing diversity with aging such that the longer one lives, the greater one's exposure to factors that affect the aging process.

The concept of linked lives and social ties is a core tenant of the Life Course Perspective. Elder (1998) theorizes that lives are interdependent and reciprocally connected in that societal and individual experiences are linked thorough the family and shared relationships. As a result, macro-level events, such as a natural disaster, could affect individual behaviors (e.g., forced migration), and this can significantly affect other familial relationships. Stressful events, such as the death of a family member, can also affect family relationships because these occurrences can trigger patterns of stress and vulnerability or, conversely, promote adaptive behaviors and family resilience. Moreover, personality attributes of individual family members can also affect overall family coping styles, functioning, and well-being.

In accordance with the Life Course Perspective, individuals are active agents with personal control, who not only alter the effect of social structure but also make decisions and set goals in ways that shape social structure (Elder, 2003). The Life Course Perspective acknowledges that the ability to make specific choices depends on opportunities and constraints (George, 2007). In this understanding of human development, early life course decisions,

opportunities, and conditions are seen to be inextricably connected to later outcomes. In this way, the past affects the future and this may occur at the cohort/generational level as well as at the individual/familial level.

The Life Course Perspective is suitable for this study because it encourages an understanding of the temporality of predictors in determining health outcomes (Elder, 2003). Three different temporal meanings are included in the Life Course Perspective: 1) chronological age, which marks developmental time and acts as an indicator or stage in the aging process, 2) social age, which looks at age patterns in social roles and timelines and 3) historical time as it relates to birth year and membership in a particular cohort that experiences history and social change at the same time (Bengtson, Elder, & Putney, 2012). Each of these three constructions of age bears unique meaning for the study of pathways through the age-differentiated life course (Elder, 2003). In addition, an understanding of critical periods throughout the life course can be built into the Life Course Perspective. Another important perspective that the Life Course Perspective adds to COD research is the understanding that COD can occur throughout the life course and can fluctuate with periods of relapse and remission, such that studying COD should also involve looking at the outcome over time, as I do. In life course research, temporality becomes part of the conceptualization of the issue, rather than just a methodological concern (George, 2007).

2.5.3 Theory of Fundamental Causes

The Theory of Fundamental Causes suggests that vast differences health outcomes and mortality (Braveman et al., 2010) result from aspects of class and social position that fundamentally underlie the more proximal causes of disease. Link and Phelan posit that an individual's "flexible resources" (e.g., wealth, knowledge/access to information, power) and

their social connections affect their health behaviors. Flexible resources affect health by determining whether or not people are aware of and can access the support necessary to avert exposure to risk factors that either lead to disease or minimize the consequences of poor health once it occurs (Link & Phelan, 1995; Phelan et al., 2010).

Unsurprisingly, individuals with high SEP have more flexible resources and social connections at their disposal to avoid health risks and adopt protective strategies, thereby producing a health advantage (Link & Phelan, 1995; Phelan et al., 2010). The flexibility of these resources is a key part of the accrued advantage: they can be adapted in different ways to different situations to accommodate the specific risk and protective factors with respect to the health outcome in question. Thus, the Theory of Fundamental Causes' formulation explains the persistent association of SEP with health over time, despite changes in the explanatory mechanisms linking these two phenomena (Link & Phelan, 1995; Phelan et al., 2010). The persistence of the association over time and its generalizability across different geographic places and vastly different health conditions suggests that no fixed set of intervening risk and protective factors can account for the connection, and thus point to underlying causes that determine a host of risk factors.

Link and Phelan define a fundamental social cause of health inequities as having four key components: 1) it must influence multiple health outcomes, not just a single disease; 2) it must affect the diseases it is associated with through multiple risk factors; 3) it must involve access to resources that help to avoid or reduce health risks or are able mitigate the aftermath of disease once it occurs; and 4) the association between it and multiple health outcomes over time must be continuously reproduced via intervening mechanisms. In this way, the overall burden of a disease may lessen over time as prevention and treatment become available, however, the

disparity in outcomes along SEP lines will not be eliminated because fundamental causes will still determine differential access to these intervening mechanisms.

The key flexible resources that are available to those with higher SEP that can be deployed to improve their health include knowledge, money, prestige and power, and beneficial social connections (Link & Phelan, 1995). To improve health, knowledge gives individuals health literacy and includes a broad array of skills and activities that are necessary to enact healthy behaviors in one's life. Money allows for the purchase of food, medication, shelter, technology, and even experiences that are associated with healthy behaviors and determines the environments that people live and work in (which similarly influence their health). Power is the ability to exert one's influence or create change, and prestige is the reputation or influence that one has, usually arising from success, achievement, or rank. Power and prestige together determine a person's place in the social hierarchy and they can be used to manifest positive health in multiple ways. For example, having power within workplace may mean the ability to take time off for well-being or to access medical treatment. Beneficial social connections garnered to someone with a high SEP allow these individuals to use their personal and professional networks for a health advantage, through having friends and colleagues who are health care providers, lawyers, or politicians who can provide advice, facilitate access to prevention and treatment, and provide material support in times of need (Phelan et al., 2010).

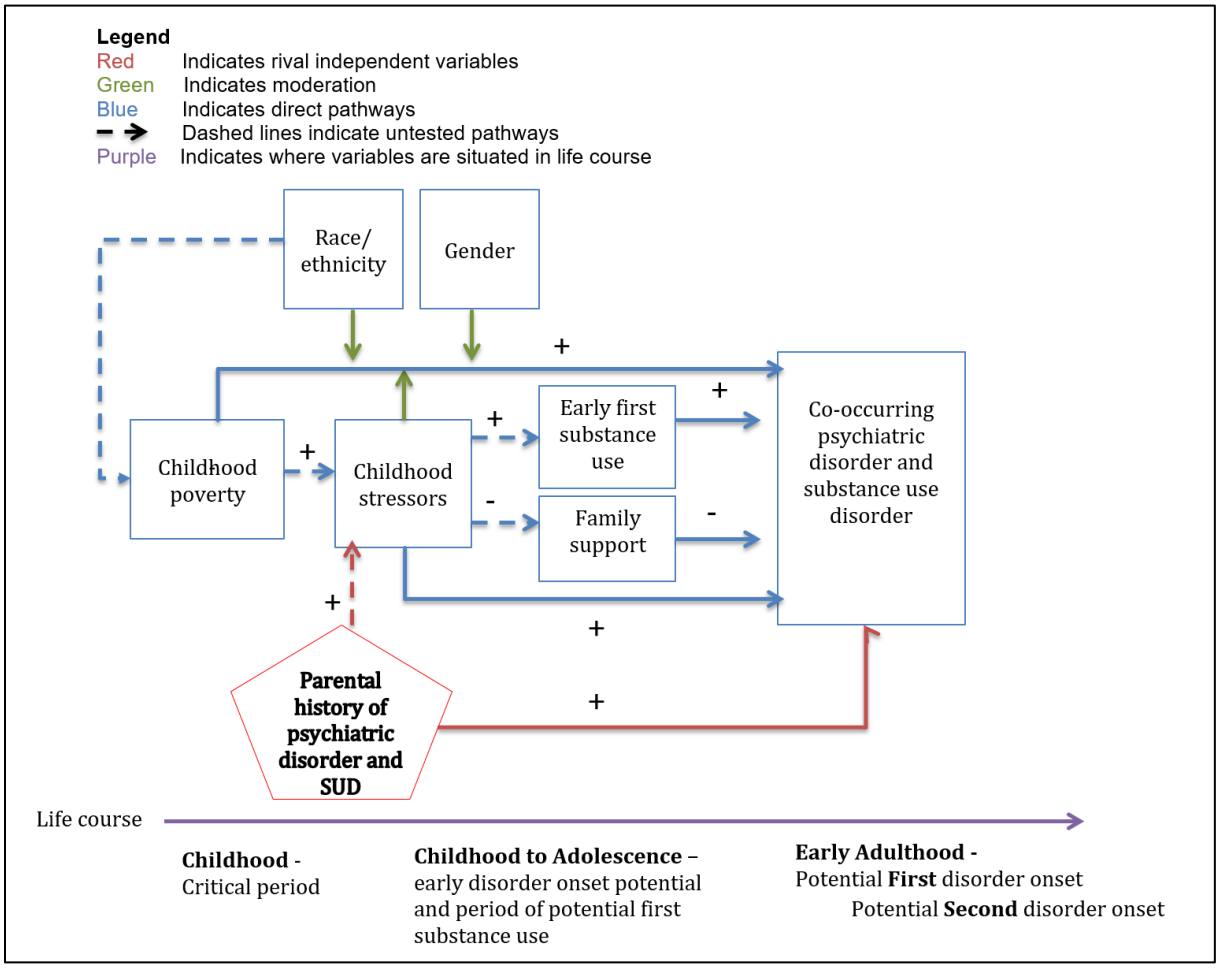
2.6 Combined Conceptual Model Used in the Dissertation

My theoretical framework for this study tests the Aims described above using a conceptual model (see Figure 2.1 below) that is informed by the Stress Process Model, the Life Course Perspective, and the Theory of Fundamental Causes. The conceptual model includes

demographics that are related to social stratification on the top left hand side, namely, race/ethnicity and gender. Demographic factors shape experiences of childhood poverty by determining both level of exposure to poverty and how harmful the effects of poverty are and, thus, it is hypothesized that the relationship between child adversity and poverty and COD differs by racial/ethnic group and by gender. Childhood poverty operates both directly and indirectly on COD in a harmful direction. Indirectly, the effect of childhood poverty on COD is expected to be partially mediated by childhood adversity, a key construct that represents stress accumulation in childhood. Despite this expectation of partial mediation, this is not testable in the current study because estimating the indirect effects with a categorical dependent and independent variable is not mathematically possible. Childhood adversity, an essential link in the chain between early life poverty and COD, also has both direct and indirect harmful effects on COD in this model. Childhood adversities are expected to intensify (i.e. moderate) the relationship between poverty and COD. Childhood stressors are also expected to operate through (i.e. be partially mediated by) risky behaviors increasing COD likelihood, such as early first substance use, and through protective factors like family support decreasing COD likelihood. Again, despite this expectation of partial mediation, this is not testable in the current study because of the categorical mediators and a categorical dependent variable. Lastly, parental psychiatric disorder, SUD, and COD are rival independent variables included to control for some of the genetic aspects of COD and shared environmental risk. Both variables are expected to have deleterious associations with childhood adversity and COD and are operationalized as family history of SUD, family history of psychiatric disorder, and family history of COD.

Figure 2.1, shown below, depicts the conceptual model for the dissertation, and shows the expected relationships between these variables.

Figure 2.1. Conceptual Model for the Dissertation



I integrate the above theories into this conceptual model in several important ways. By adding time explicitly into this conceptual framework, through the connection between early life events and later life outcomes, I am using the Life Course Perspective. Specifically, I test select ways in which timing influences COD outcomes through "critical" periods during which events can be particularly impactful on COD (Papachristou et al., 2013), like early first substance use and stressors that happen before age 18. I draw on the concept of linked lives from the Life Course Perspective to understand the way in which parental characteristics and behaviors influence their children's mental health later in life. I use the Life Course Perspective to ensure

that childhood poverty and childhood stressors are properly contextualized and situated within an understanding of their roles in the development of adult substance use and psychiatric disorder and the way these adversities build over time by studying different forms of the childhood stressor measures.

In this model, the critical period is childhood (before age 18) and the milestone of timing of first alcohol or substance use is considered. Aim 3 tests the impact of childhood poverty and other stressors on timing of COD, and incorporates many life course principles through an explicit focus on timing and risk.

Including the Stress Process Model in this comprehensive model gives structure to the Life Course Perspective and facilitates predictions about the way in which childhood poverty (mediated through increased risks/stressors and diminished access to flexible resources, termed such by the Theory of Fundamental Causes) leads to the development of COD. The Stress Process Model tests specific mechanisms and pathways linking childhood poverty, childhood stressors, and COD and this theory supports Aims 1 and 2 of the study. I incorporate an understanding of the sociological study of stress with my attention to the way that status characteristics regulate stress exposure. In addition, by combining concepts from the Stress Process Model and Life Course Perspective together, I assume the process of stress accumulation is inherently temporal and involves interactions between stressors or resources and social position over time.

The Theory of Fundamental Causes provides a theoretical rationale for the hypothesized relationship between poverty in childhood and COD in adulthood, as those who grow up in poverty are likely to have less access to flexible resources that they can deploy (or that their parents can deploy on their behalf) to counter the threats to mental health. Additionally, this

theory supports the examination of multiple substance use and psychiatric disorders, rather than just a single disorder, with the expectation that the underlying access to resources and social support will influence the disorders being examined in harmonious ways.

In conclusion, the Stress Process Model, Life Course Perspective, and Theory of Fundamental Causes add considerable depth and structure to the proposed study and have guided the development of research Aims and methods addressing the underlying causes of disorder, timing, and the accumulation of stress in a nuanced way.

2.7 Variations in COD by Race/Ethnicity and Gender

Each of this study's three Aims have hypotheses formulated to test for variation by gender and race/ethnicity. The base model I have proposed is expected to operate differently for different social groups based on previous race/gender conditional relationships seen with the social determinants of individual disorder. These groups under study also have markedly different susceptibility to disorders overall, as well as to different disorder types.

I expect males to be more affected by childhood poverty than females in terms of developing COD because males have been shown to be psychologically impacted by family economic insecurity in other studies (Conger et al., 1992). This may occur partially because of adults' socializing responses to misbehavior in males at young ages. Zahn-Waxler and colleagues propose that misbehaving is a characteristic more common in low-income males that gets exacerbated when adults reprimand and punish aggressive behaviors in these young males more harshly that their higher-income counterparts (Zahn-Waxler et al., 2008), and in doing so they may inadvertently intensify the impacts of poverty on disorder.

Alternatively, I expect females to be more affected by childhood household adversities than males, including child sexual abuse, because females tend to value caregiver bonds more highly, take on more familial stress, and incur more mental burden in dysfunctional home environments than their male counterparts (Zhan-Wexler et al., 2008).

I expect childhood stressors, specifically child sexual and physical/verbal abuse, to be more strongly associated with COD in non-Hispanic Whites compared to all other racial/ethnic groups. I hypothesize this because even though racial/ethnic minorities will have higher exposure to many of these stressors, the strong coping mechanisms and familial social, cultural, and religious support described in the Hispanic (Moos & Moos, 2007), non- Hispanic Black (Staton-Tindall, 2013), and Asian American (Sue et al., 2012) communities assist in developing resilience to harmful psychological and substance use outcomes. For the same reasons, I hypothesize that childhood poverty will be more strongly associated with COD in non-Hispanic Whites compared to all other racial/ethnic groups.

2.8 Chapter Summary

Chapter 2 outlined the research Aims and questions that are under examination in this dissertation, setting up the hypotheses that are tested in the study and providing a theoretical basis for the investigation. I introduced the reader to the Stress Process Model, the Life Course Perspective, and the Theory of Fundamental Causes, reviewing the relevance of each for the study of childhood poverty, childhood adversity, and COD. Finally, I presented the conceptual model designed specifically for this study and explain why the relationships under study are expected to vary by gender and by race/ethnicity.

CHAPTER 3: RESEARCH DESIGN AND METHODOLOGY

The third chapter of this dissertation begins by outlining the data source: describing the data set used, the sampling procedures, and the parent study eligibility criteria. Then, I review the variables used in the dissertation, and describe the analysis plan for each Aim that was presented in Chapter 2, showing the models and equations that are tested throughout the study and specifying how I will reject or fail to reject hypotheses. I review missing data and comment on the ability to assume data are missing at random.

3.1 Data Set Description

The National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III) was sponsored, designed, and directed by the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The NESARC-III is a cross-sectional survey conducted with a nationally representative sample of the civilian non-institutionalized population of the United States aged 18 years and older in 2014. NESARC-III is the third wave of the NESARC national survey that NIAAA has conducted. Although the objectives and substantive material included in NESARC-III remains similar to earlier versions, Wave III is a new sample and is not longitudinally connected to Waves I or II (Grant et al., 2015).

3.2 Study Eligibility

To be eligible for sample selection in NESARC Wave III, individuals had to be 18 years or older at the time of screening as well as not currently on active duty in any of the US Armed Forces, Military Reserves, or National Guard (Grant et al., 2015). They also had to be residents of the 50 states and reside in a household or select group housing (e.g., college dormitories).

Institutionalized persons were excluded.

3.3 Sampling Procedures

The following detailed description of the sampling procedures was obtained from study documentation by Grant and colleagues (2015). The sample was derived using multi-staged probability sampling to randomly select persons from the eligible population. Primary sampling units (PSUs) were first selected and were either individual counties or groups of contiguous counties. From the sampling frame of 2,349 PSUs, 150 were selected using stratified proportional-to-size sampling. A measure of size calculation (Folsom, Potter & Williams, 1987) was applied to each PSU to obtain self-weighting samples of the ultimate sample units (households). This also ensured that approximately equal numbers of dwelling units were selected per PSU.

Secondary sampling units were then selected at the level of census blocks. The 2010 Census Summary File block data file was used to generate a complete list of segments for the purpose of creating a sampling frame within each of the 150 sample PSUs. For NESARC-III, a segment consisted of either an individual census block or a combination of two or more nearby blocks. Segments were created using proprietary software developed by Westat, a statistical survey research corporation hired to provide research services for NESARC. The segment creation process is described in greater detail in the study documentation (Grant et al., 2015).

In the third stage of sampling, households within the sampled secondary sampling units were selected. A total of 71,052 addresses were selected for the sample. The selected households were derived from master address files created and maintained by the US Postal Service. Although the within-segment sampling rate varied by segment, it yielded a sample of 9 to 10

addresses per segment prior to exclusions or non-response (Grant et al., 2015).

The last stage of sampling involved random selection of eligible adults within the sampled households. In households with three or fewer eligible persons, only one sample person was selected. In households with four or more eligible persons, two persons were selected. Selecting more than one person in the larger households in the NESARC sample was allowed to increase efficiency without unduly inflating design effects resulting from clustering, and also to give minority household members slightly higher chances of selection. The interviewer collected the relationship of each household member to each sample person using a screener that could be administered to any household member aged 18 or older. Spanish, Mandarin, Cantonese, Korean, and Vietnamese versions of the screener and subsequent interview materials were administered by certified bilingual interviewers in households where the members preferred to take the interview in one of those five languages. Areas of the United States with a high percentage of Spanish-speaking and Asian language-speaking households were sampled at a higher rate than areas with lower percentages of these language speakers. The final sample size was 36,309 and included persons living in households and select non-institutional group quarters (Grant et al., 2015).

3.4 Data Collection Procedures

Westat designed and conducted the data collection process. Computer-assisted personal interviewing (CAPI) was the method of data collection. A CAPI screener collected household information and selected one or two members of the household for participation in the NIAAA NESARC-III study. A consent module was then used to document official informed consent for study participation and an incentive module followed consent to document the incentive payment

provided to individuals who agreed to complete the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-5). The AUDADIS-5 was developed to assess alcohol, drug and mental disorders according to diagnostic definitions embodied in the *Diagnostic and Statistical Manual of the American Psychiatric Association, 5th Edition (DSM-5*; American Psychiatric Association, 2013) in both clinical and general populations. Both the reliability and validity of the AUDADIS-5 in substance use and psychiatric disorder diagnoses were found to be fair to excellent (Grant et al., 2015; Hasin et al., 2014). The AUDADIS-5 was developed based on previous versions of the AUDADIS that had been extensively tested for reliability and validity (Ruan et al., 2008).

Interviewers were trained in proper survey administration techniques that were applied to the full NESARC-III data collection process using five methods of training: home study, demonstration, interactive lecture, practice exercises, and dyad role-playing. Additionally, the training focused on the sensitive nature of the questions asked in the AUDADIS-5 interview and the sensitivity required to administer them. Interviewers were required to have a minimum of a high school diploma or general educational development certification, as well as previous interviewing or public contact experience, and to be available to work a minimum number of hours, including evenings and weekends. Bilingual interviewers fluent in the languages of survey administration were encouraged to apply.

3.5 NESARC-III Dataset

The dataset contains self-report data on psychiatric disorder and substance use, demographics, physical health, well-being, and mental health treatment utilization. The NESARC-III study collects the substance use and psychiatric disorder information necessary to

indicate a probable diagnosis rather than asking respondents whether or not they have ever received a formal diagnosis. This is a strength of the dataset as it allows for diagnostic criteria to be captured without being compromised by access to health care, as is the case with reliance on self-report of disorder diagnosis. The AUDADIS-5 interview contains the following sections: *Background information and family history questions* (with questions on personal and demographic background, childhood experiences, and family history); *Alcohol experiences* (with questions on alcohol consumption, experiences with alcohol, and alcohol/drug treatment utilization); *Tobacco and drug use experiences* (with questions on tobacco and nicotine use, drug use, and experiences with drugs); *Psychiatric disorders* (with questions on mood, anxiety, usual feelings and actions, behavior, and traumatic experiences); and *Physical health* (with questions on medical conditions and low weight, eating, and over-eating). Answers to screening questions were used to determine which subsequent questions should be asked/skipped for each respondent, and this process was automated with the CAPI program.

3.5.1 Data Permissions & Human Subjects Approval

The research protocol for NESARC–III, including its informed consent procedures, received full ethical review and approval from the US Census Bureau and the US Office of Management and Budget. The UCLA South Institutional Review Board reviewed and approved my proposal for research using the NESARC-III data on July 14, 2016, as an Expedited application (IRB#: 16-001072). To access the data in accordance with NIAAA policy, I submitted a data analysis proposal and data use agreement to the NIAAA. The agreement was approved on October 6, 2016.

3.6 Strategies to Minimize Non-Response

To improve respondent cooperation, all sampled addresses received an advance letter and

study brochure approximately 1-2 weeks before the interviewer attempted the initial visit. Other strategies employed to increase response rates included: sending nonresponse letters and postcards, mailing a hardcopy paper version of the screener, administering the screener via telephone if necessary, revising the design of the interviewer badge, and implementing interviewer incentive programs.

Data collection occurred in three overlapping stages: the initial phase, the re-assignment phase, and the special nonresponse conversion phase. In the initial phase, cases were assigned by the supervisor to an interviewer on the basis of the demographic composition of the area and the proximity of the segment to the interviewer's home. In this phase, interviewers made up to four in-person calls to the household to complete a screener, and up to four additional in-person contacts (after completing the screener) to administer the AUDADIS-5 interview and saliva collection. Once the prescribed number of in-person attempts had been reached, the interviewer consulted the regional supervisor to determine further contact strategies. The initial phase was complete when the interviewer reported a definitive outcome (e.g., refused) for the case or when the full number of attempts had been made.

During the reassignment phase, cases not resulting in completed interviews during the initial phase were reviewed by the regional supervisor. After the review and troubleshooting of incomplete interviews had been completed, incomplete cases were assigned to another interviewer in the same or nearby PSU. In the special nonresponse conversion phase the field management team assembled a special traveling team of the most experienced or productive interviewers to perform a nonresponse conversion effort under the supervision of the field supervisors. To maximize the success, most contacts were attempted between 3 p.m.-9 p.m. on weekdays and 10 a.m.-9 p.m. on weekends. Contact attempts at each address were scheduled on

five different days of the week and at different times of day.

3.7 Study Variables

Variables used in this study are based on the conceptual model illustrated in Figure 2.1. The focal independent variable is childhood poverty. The focal dependent variable is lifetime co-occurring psychiatric disorder and SUD, defined as occurrence of each disorder at any point during the life course. Other variables included in the models are: demographics (race/ethnicity; gender; nativity status; and age), family characteristics (family support; family history of any psychiatric disorder, substance use disorder, and COD; and family composition during childhood) and childhood experiences (three measures of childhood adversity, age of first substance use). The variables are presented below based on their role in the analyses. Frequency distributions of the variables of interest will be discussed in *Section 4.1 Sample Characteristics* on page 93 and can be found in Tables 4.1, 4.2, and 4.3.

3.7.1 Dependent Variables

Co-occurring Psychiatric Disorder and Substance Use Disorder. The focal dependent variable used in Aims 1 and 2 is a categorical variable indicating lifetime COD status by using lifetime diagnosis of *DSM-5* for both SUD and psychiatric disorder. Regarding the former, lifetime diagnoses include alcohol use disorder, or all other drug use disorders except tobacco use disorder (including marijuana use disorder, cocaine use disorder, heroin use disorder, etc.). For psychiatric disorders, lifetime diagnoses include at least one of the following conditions: major depressive disorder (hierarchical), mania, specific phobia, social phobia, panic disorder, agoraphobia, generalized anxiety disorder, posttraumatic stress disorder, anorexia nervosa,

bulimia nervosa, antisocial personality disorder, conduct disorder, borderline personality disorder, and schizotypal personality disorder.

The focal dependent variable of COD is operationalized using a definition of lifetime occurrence of both a psychiatric disorder and SUD for the main analyses: meaning that the two disorders do not need to occur at the same time for the person to have a COD. This variable contains four possible categories: "COD," "psychiatric disorder only," "SUD only," and "no disorder." That is, a person would be classified as having "COD" on this measure if they were to have both types of disorder at any point in their lifetime, "psychiatric disorder only" if they had a psychiatric disorder in their lifetime but no SUD, "SUD only" if they had SUD in their lifetime but no psychiatric disorder, and "no disorder" if they had no lifetime history of either psychiatric disorder or SUD. The temporality and/or overlap of the disorders are not considered in this operationalization; only that the two types of disorder need to both occur for 'COD' classification. This operationalization was chosen for three reasons: 1) data are not available to determine all possible overlap of disorders temporally; 2) lifetime co-occurrence acknowledges that disorders can impact an individual without necessarily happening simultaneously; and 3) this operationalization maximizes the analytic sample when compared to the restricted window of observation available for studying temporally overlapping disorders in NESARC-III.

Co-occurring Psychiatric Disorder and Substance Use Disorder – Alternative Definition. Sensitivity testing of the significant conditional relationship in the results for Aims 1 and 2 with an alternative definition of co-occurrence was conducted. Specifically, COD was alternatively defined as temporally overlapping psychiatric disorder and SUD in the year prior to data collection to test if the patterns detected hold true for those with temporally overlapping disorders. As previously indicated, NESARC-III does not collect time and duration information

for all disorders only timing and duration of: the first occurrence of each disorder, the most severe occurrence of each disorder, the most recent occurrence of each disorder, and every disorder happening in the year prior to data collection. Sensitivity testing with temporally-overlapping COD only during the year prior to data collection is thereby possible and was conducted to test the persistence of findings with temporally overlapping COD. This definition applies a more restrictive analysis that is more closely aligned with the definition used in clinical research. Notably, it does not take into account that someone may have previously had a different disorder status than they do in the year prior to data collection.

This variable contains four possible categories: "recent COD," "recent psychiatric disorder only," "recent SUD only," and "no recent disorder." A person is classified as having "recent COD" on this measure if they have both types of disorder in the year prior to data collection, "psychiatric disorder only" if they had a psychiatric disorder in the year prior to data collection but no SUD, "SUD only" if they had SUD in the year prior to data collection but no psychiatric disorder, and "no disorder" if they had no lifetime history of either psychiatric disorder or SUD.

Age of Onset of Co-occurring Psychiatric Disorder and Substance Use Disorder. The dependent variable for the Aim 3 analyses is the age at which respondents have their second disorder (for those who have two). For the survival analyses conducted in Aim 3, the time period studied is the period from birth until someone develops a COD, marked by the age at which they develop their second type of disorder. For example, if an individual developed major depressive disorder at age 21 and alcohol use disorder at age 22, their age of onset for COD would be age 22.

The variable for age of onset of COD does not have four categories, as the lifetime

definition used in Aim 1 and Aim 2 does. The variable for age of onset of COD is simply composed of the age at which the respondent first develops the second disorder type and does not take into account a differentiation of those who have only one type of disorder from those with no disorder.

The failure variable in this model is a binary variable that captures lifetime COD (Yes=1/ No=0), and the model accounts for the time between the starting period (birth) and the determination of the outcome. For those who have not yet developed COD by the time they are interviewed, they remain at risk for the entire duration of the study and their observation is censored at the age of interview.

Note that this variable by design groups together all other outcomes in the "no lifetime COD" group including those with no disorder, those with psychiatric disorder only, and those with SUD only. This is an essential concession because developing a first disorder is a necessary but not sufficient criteria for developing COD, and including a variable that accounts for the development of a first disorder is too highly predictive of the outcome of COD, such that including it obscures the relative hazard of other variables.

The questions for behaviors related to borderline personality disorder and schizotypal personality disorder were prefaced with the phrase, "beginning in early adulthood," and age of onset was not asked. Therefore, because of the way this question limited age of onset answers, these two disorders are excluded from the dependent variable in the Aim 3 analysis. All other psychiatric disorder and SUD listed in the above COD definition were included in the age of onset for COD variable.

3.7.2 Key Independent Variables

Childhood Poverty- focal independent variable. Childhood poverty, the focal independent

variable, is measured with the following question: *"*Before you were 18 years old, was there ever a time when your family received money from government assistance programs like welfare, food stamps, general assistance, Aid to Families with Dependent Children, or Temporary Assistance for Needy Families?" This question is coded as a dichotomous yes=1 /no=0 variable. There is an additional question for those who are positive on the childhood poverty variable that asks, "About how many years altogether between the time you were born and the time you turned 18 did your family receive money from a government assistance program?" This variable has a large amount of missing data (n=1,214 missing) and is not used in the analysis. Exposure to poverty in childhood is thus captured as a dichotomous yes=1 /no=0 variable.

Childhood Adversities –moderator and control variable. Childhood stressors are covered in a set of twenty-four questions asking about experiences before age 18 and includes questions about how the parent/caregiver/ household member treated the respondent, questions about how other adults treated them, and questions about experiences that happened to any other adult living in the home. The questions for this section can be seen in Table 3.1, which shows the childhood adversity variables, the categories of adversity they represent, and the questions and answer text for each.

The questions about parental treatment, for example, are prefaced by the statement: "The next few questions are about how your parents or caregivers treated you while you were growing up, that is, BEFORE you were 18 years old." Questions then proceed to ask how often events happened with the response options, "0 = never," "1 = rarely," "2 = sometimes," "3 = often," and "4 = very often." The caregiver questions include eighteen items that ask about sexual abuse, verbal abuse, physical abuse, neglect, and domestic violence. The other six questions ask about experiences that happened to any adult in their household before the child was 18 including

imprisonment, alcohol or drug use causing problems, hospitalization for psychiatric disorder, and suicide attempts and outcomes.

Table 3.1 Childhood Adversity Measures Text

Category	Variable Name	Question	Response Option
Neglect	Neglect1	How often were you made to do chores that were too difficult or dangerous for someone your age? [a]	0. Never 1. Almost never 2. Sometimes 3. Fairly often 4. Very often
	Neglect2	How often were you left alone or unsupervised when you were too young to be alone, that is, before you were 10 years old? [a]	
	Neglect3	How often did you go without things you needed like clothes, shoes or school supplies because a parent or other adult living in your home spent the money on themselves? [a]	
	Neglect4	How often did a parent or other adult living in your home make you go hungry or not prepare regular meals? [a]	
	Neglect5	How often did a parent or other adult living in your home ignore or fail to get you medical treatment when you were sick or hurt? [a]	
Verbal abuse	Verbal Abuse1	How often did a parent or other adult living in your home swear at you, insult you or say hurtful things? [a]	0. Never 1. Almost never 2. Sometimes 3. Fairly often 4. Very often
	Verbal Abuse2	How often did a parent or other adult living in your home threaten to hit you or throw something at you, but didn't do it? [a]	
	Verbal Abuse3	How often did a parent or other adult living in your home act in ANY other way that made you afraid that you would be physically hurt or injured? [a]	
Physical abuse	Physical Abuse1	How often did a parent or other adult living in your home push, grab, shove, slap or hit you? [a]	0. Never 1. Almost never 2. Sometimes 3. Fairly often 4. Very often
	Physical Abuse2	How often did a parent or other adult living in your home hit you so hard that you had marks or bruises or were injured? [a]	
Sexual abuse	Sexual Abuse1	How often did an adult or other person touch or fondle you in a sexual way when you didn't want them to or when you were too young to know what was happening? [b]	0. Never 1. Almost never 2. Sometimes 3. Fairly often 4. Very often
	Sexual Abuse2	How often did an adult or other person have you touch their body in a sexual way when you didn't want to or you were too young to know what was happening? [b]	
	Sexual Abuse3	How often did an adult or other person attempt to have sexual intercourse with you when you didn't want them to or you were too young to know what was happening? [b]	
	Sexual Abuse4	How often did an adult or other person actually have sexual intercourse with you when you didn't want them to or you were too young to know what was happening? [b]	

Domestic violence	Domestic Violence1	Push, grab, slap or throw something at her? [a,c]	0. Never 1. Almost never 2. Sometimes 3. Fairly often 4. Very often
	Domestic Violence2	Kick, bite, hit her with a fist, or hit her with something hard? [a,c]	
	Domestic Violence3	Repeatedly hit her for at least a few minutes? [a,c]	
	Domestic Violence4	Threaten her with a knife or gun or use a knife or gun to hurt her? [a,c]	
Parental events/ circumstances	Parental Drinking	BEFORE you were 18 years old, was a parent or other adult living in your home a problem drinker or alcoholic? [d]	1. Yes 2. No
	Parental Drugs	BEFORE you were 18 years old, did a parent or other adult living in your home have some similar problems with drugs? [d]	
	Parental Incarceration	BEFORE you were 18 years old, did a parent or other adult living in your home go to jail or prison? [d]	
	Parental Psychiatric Hospitalization	BEFORE you were 18 years old, was a parent or other adult living in your home treated or hospitalized for a mental illness? [d]	
	Parental Suicide Attempt	BEFORE you were 18 years old, did a parent or other adult living in your home attempt suicide? [d]	
	Parental Suicide Success	BEFORE you were 18 years old, did a parent or other adult living in your home actually commit suicide? [d]	

[a] Preface to the questions was "The next few questions are about how your parents or caregivers treated you while you were growing up, that is, BEFORE you were 18 years old. By parents or caregivers, I mean your mother, father, stepmother, stepfather, adoptive mother or father, foster parent or other adult living in your home."

[b] Preface to the question was, "Now I'd like to know if you had any of the following sexual experiences with an adult or any other person BEFORE you were 18 years old. By adult or other person I mean a parent, stepparent, foster parent, adoptive parent, a relative, friend, family friend, teacher or stranger."

[c] Preface to the questions was, "How often did your father, stepfather, foster or adoptive father or mother's boyfriend do ANY of these things to your mother, stepmother, father's girlfriend, or your foster or adoptive mother?"

[d] Qualifier to the question was, "By alcoholic or problem drinker, I mean a person who had physical or emotional problems because of drinking; problems with a spouse, family, or friends because of drinking; problems at work or school because of drinking; problems with the police because of drinking – like drunk driving; or a person who seemed to spend a lot of time drinking or being hung over."

A simple summative scale of adversities has the potential to mask the nature of the relationship between specific adversities and psychiatric disorders (Schilling et al., 2009). Therefore, I examined three different ways of categorizing and operationalizing the childhood stressors including: 1) creating a summative score of the number of adverse experiences that ever happened before 18; 2) grouping the number of stressors by "types" of events (including physical abuse, verbal abuse, sexual abuse, neglect, domestic violence, and parental events), and 3) conducting a latent class analysis to study underlying classes of stressors that are likely to co-occur in the population. I then studied the distributions of the three different operationalizations and analyzed their bivariate associations with COD to determine how different adversity classifications affect the conclusions drawn about childhood adversity and COD. This investigation and the details about the different operationalizations tested appear in *Section 4.2 The Measurement of Childhood Adversity* on page 111.

Based on the preliminary analyses and investigations of the childhood adversity variables, I selected three variables to capture the experience of stress before age 18: a summative score of number of experiences that ever occurred during childhood (range 0-20; truncated at 15 due to a long tail), a measure of sexual abuse frequency, and a combined measure of verbal and physical abuse frequency. The three final measures are described below:

- The first measure used for childhood adversities is a summative score of experiences (each coded as yes = 1 / no = 0) that ever occurred during childhood (observed range 0-20; truncated at 15 due to a long tail)
- Frequency of sexual abuse was calculated by taking the average of the frequencies reported for each of the four sexual abuse variables (reported on a scale of 0-4 where 0 represented "never" and 4 represented "very often").

- Frequency of verbal/physical abuse was calculated by taking the average of the frequencies reported for each of the verbal and physical abuse variables (five variables, also reported on a scale of 0-4 where 0 represented "never" and 4 represented "very often").

Race/ethnicity –moderator and control variable. Race/ethnicity is tested for its role as a potential moderator in several hypotheses. The race/ethnicity variable was created using five race categories: White, non-Hispanic; Black, non-Hispanic; American Indian/Alaska Native, non-Hispanic; Asian/Native Hawaiian/Other Pacific Islander, non-Hispanic; Hispanic, any race. The American Indian/Alaska Native Category was dropped in the analyses conducted for this study due to the small sample size and high rates of disorder indicating a unique population (n = 511), leaving the final variable to include four possible race/ethnicity categories. Non-Hispanic Whites are the reference group in the estimated models.

Gender –moderator and control variable. Gender is included and is tested for its role as a potential moderator in several hypotheses. The gender variable is a dichotomous male/female (male=1 /female=0) variable, in accordance with the way it was collected.

Disorder sequence –moderator and control variable. The variable for disorder sequence is included only in some of the models estimated for Aim 3 of this study. Disorder sequence is tested for its role as a potential moderator in Hypotheses 3c-3f. The disorder sequence variable is a dichotomous psychiatric disorder /SUD (psychiatric =1 /SUD =0) variable and it only includes those with at least one disorder, indicating either which disorder type respondents have in their lifetime, or which they developed first (if they have COD). For the small number of respondents who had psychiatric disorder and SUD onset within the same year (n=398) where it was not possible to distinguish the precise order of onset I assigned them to the psychiatric disorder

category because psychiatric disorder is more likely to onset before SUD, overall. I repeated the analysis with these individuals assigned to the SUD category to ensure this coding decision did not impact the results substantively.

3.7.3 Rival Independent Variables

Family History of Psychiatric Disorder, SUD, and COD – rival independent variables. For the rival independent variables of parental history of COD, SUD, and psychiatric disorder, questions were taken from the family history sections of the NESARC-III questionnaire. The presence or absence of family history captures additional information compared to the measure of disorders in adult caregivers that have adverse impacts during childhood for the children (a measure of which is included in the childhood adversity section above). The family history variables included as rival independent variables also include disorders not captured in the childhood adversity question, such as disorders that did not affect family functioning, and disorders that occurred for the first time after the child turned 18.

Several questions were combined to determine the presence of maternal and paternal history of SUD, psychiatric disorder, and COD, such as, "Has your blood or natural mother been an alcoholic or problem drinker at ANY time in her life?" and "Was your blood or natural father depressed at ANY time in his life?" Family history questions queried mood and anxiety disorders, personality disorders, alcohol use disorders, and other SUD. The family history variables used include 4 binary variables each coded as yes = 1 / no = 0 for any maternal or paternal history. The four variables are

1) SUD only history: this variable includes two categories, in the absence of psychiatric disorder: (0) mother or father with no history of SUD, (1) mother or father with history of SUD;

2) Psychiatric disorder only history: this variable includes, in the absence of SUD: (0) mother or father with no history of psychiatric disorder, (1) mother, father, or both with psychiatric disorder history;

3) COD history: this variable includes two categories: (0) no mother or father with COD history, (1) mother, father, or both have COD history;

4) Unknown family history: this variable includes two categories: (0) mother or father's history is known, (1) mother or father's history is unknown.

The definition of lifetime co-occurrence used in the dependent variable was retained here where lifetime presence of a psychiatric disorder and SUD in a parent indicated co-occurrence.

3.7.4 Control Variables

Demographic Variables – control variables. Nativity status is included to capture whether respondents were born in the United States or not (yes=1 /no=0). Age is included in the analyses as a continuous variable ranging from age 18-90.

Family Structure – control variable. Questions about family structure from the demographic section were combined to create a variable that describes the respondent's childhood household before the age of 18. This variable is used to control for the structure of the household that the respondent grew up in, which may have an influence on their adult mental health. The resulting family structure variable is a categorical variable with 4 categories: two biological parents, single parent, reconstituted families (biological parent with a step-parent), and all other arrangements. The reference category is two biological parents when used in multivariate models.

Family Support – control variable. Family support is an important control variable, as support is a resource and can reduce the impact of stressors on mental health. The family support

variable came from a set of five questions that ask how often before the age of 18 the respondent felt there was someone in the family: who wanted them to be a success, someone who helped them feel important or special, was a source of strength, and believed in them. It also questions whether the respondent felt they were part of a close-knit family. Frequency for these questions was asked on a scale from 0 ("never") to 4 ("very often").

A mean family support score was first created by adding the mean responses for all five questions to capture the level of family support perceived by participants before age 18; however, due to the high levels of support and the skew on this variable, a dichotomous variable is instead used to capture whether or not support was present. The resulting variable for family support is a dichotomous yes = 1 / no = 0 variable where "yes" includes any respondents that scored "very often" on any of the questions asked and "no" includes respondents that did not score "very often" on any of the questions asked.

Alcohol and Substance Use Initiation – control variable. Early first use of alcohol or drugs is associated with likelihood of SUD and is controlled for. For early initiation of substance use, several variables were combined that asked, "About how old were you when you first started drinking, not counting small tastes or sips of alcohol?" And, "About how old were you when you first started [doing drugs]?" The earliest age cited of all the questions asking about alcohol and drugs was used, producing a continuous variable. For those who could not recall an exact age, an approximate age was used. For those who never drank alcohol or never used any drugs (n = 3,927), their current age was used to avoid excluding them from the models due to missing data on this variable.

3.7.5 Treatment of Missing Data

Missing data for 19 measures in the background characteristics were addressed by NESARC through imputation of missing responses. For each imputed variable, the data file contains an associated "flag" variable that is coded with a value of "1" if the value of the variable was imputed. The only variable relevant to this analysis that NESARC imputed is respondent age. Age was imputed by NESARC for 1.13% of responses using both assignment and allocation where it was assigned based on other reported age or allocated based on sex and age interval (interviewers estimated age if respondents refused to provide their age). No responses are missing on age at first substance use, race/ethnicity, gender, family configuration, or nativity status.

Missing data on three other variables used in the study was handled with listwise deletion of those respondents with missing data, because missing data comprised only 5% of the sample (Schafer, 1999; Bennett, 2001). The variables that were missing data included: family support (missing n = 156), childhood adversity (n = 1,373), and childhood poverty (n = 781).

Logistic regression was used to determine whether those respondents missing responses on study variables differ from those who have complete information. See results of the missing analysis in Table 3.2 below, which shows the results for the three logistic regressions conducted to determine the correlates of missing data for family support, childhood adversity, and childhood poverty. Looking at this table, it is clear that data are not missing at random for any of the variables examined. Demographic differences are seen overall between those who did and did not respond to the three respective questions. Trends across all three variables for missing data include age differences in those who did and did not respond to questions, as well as race differences in the respondents for two of the three variables. Those with an "other" family

structure were less likely to respond to all three questions, and education differences were also seen across the board: those with more education were less likely to be missing. Specific information about characteristics of respondents with missing data is given below.

Table 3.2 Logistic Regression of Missing on Study Variables on Demographic Categories

	Model 3.1a: Missing on Childhood Adversity n=35,798			**Model 3.1b**: Missing on Childhood Poverty n=35,798			**Model 3.1c**: Missing on Family Support n=35,798		
Characteristic	Odds Ratio		SE	Odds Ratio		SE	Odds Ratio		SE
Age (years)	1.016	***	0.002	0.994	*	0.003	1.017	*	0.007
Male (/female)	1.013		0.066	1.259	*	0.119	0.998		0.184
Race (/NH White)									
NH Black	1.487	***	0.133	1.486	***	0.155	1.131		0.314
NH Asian	1.572	*	0.282	1.219		0.316	2.161		0.898
Hispanic	1.176		0.172	1.159		0.150	0.839		0.253
US-Born (/foreign born)	0.833		0.094	1.958	***	0.345	1.339		0.397
Childhood family structure (/two biological parents)									
Reconstituted families	2.493	***	0.239	1.868	***	0.203	1.389		0.324
Single parent	2.352	***	0.223	1.705	***	0.210	1.048		0.323
Other	28.906	***	3.186	2.965	***	0.520	3.220	*	1.625
Education Category (/<high school)									
High school or GED	0.837		0.098	0.781		0.128	0.637		0.193
Some college	0.758	*	0.088	0.723		0.120	0.684		0.217
College or associate degree	0.689	**	0.083	0.690	*	0.101	0.503	*	0.134
More than college	0.686	*	0.124	0.409	***	0.084	0.387		0.215
Household Income ($/year)	0.966	***	0.009	0.982		0.011	0.983		0.021
Model Statistics	F= (14,100)	***	81.12	F= (14,100)	***	18.85	F = (14,100)	***	6.41

Note: SE = Linearized standard error, NA = Not applicable

* p<.05; ** p<.01; *** p<.001, conservative criteria of significance not applied to missing analyses

This lack of randomness in the missing information presents a concern and bias that may be introduced to the study. Those missing childhood adversity data were more likely to be Black

(than White), to be born outside of the US (than inside the US), and to have grown up in reconstituted or "other" family configurations. Also, missing information regarding this variable was negatively associated with age and household income, and positively associated with education. Those missing childhood poverty data were more likely to be: male (than female), Black, born in the US, and to have grown up with family configurations that are single parent, reconstituted, or "other." Missing on childhood poverty data was negatively associated with education and age. Missing on family support data was positively associated with age, and having had childhood family configurations in the "other" category. Those missing data on the dependent variable of age at first onset of disorder (n = 1,132 for Aim 3) were excluded from the Aim 3 analysis only.

This lack of randomness in the missing data means that the analysis for this study will be less likely to be accurately representative of those who are Black, male, have lower SEP, as well as those who grew up in "other" family configurations, overall, as these groups were more likely to be missing data for multiple variables. The estimates for the specific variables with missing data above will be biased in their tendency to accurately represent associations for those with complete data.

3.8 Analytic Plan for Preliminary Analyses

3.8.1 Plan for Assessment of Missing Data

All analyses were done using Stata® version 14 (StataCorp, 2016) and MPlus version 7.4 (Muthén & Muthén, 2015). The first step taken in the preliminary analyses was to assess the missing data for each variable used in the study. Data were missing for the following variables: family support, childhood poverty, and childhood adversity. Weighted logistic regression

analyses were conducted comparing demographic characteristics of those who were missing data from those who were not missing data for each of these variables to assess the extent to which bias was introduced in the study from missing data. The results of this assessment of missing data and the determination of the extent to which data are missing at random appears above on page 65.

3.8.2 Plan for Preliminary Analyses Preceding Multinomial Logistic Regression

Multinomial logistic regression is used to answer research questions in Aim 1 and Aim 2. As others in the literature have noted, an incremental process of model building for conducting multivariate regression with survey data appropriately includes: (a) estimation of bivariate associations between the independent variables and the dependent variable, (b) retention of the independent variables statistically significant at the $p \leq .05$ level as candidates for the multivariate model, (c) testing the overall significance of each independent variable in the multivariate model using the Adjusted Wald test, and (d) examination of hypothesized interactions among the independent variables (Hosmer & Lemeshow, 2000; Heeringa et al., 2010 in Aneshensel, 2012).

The preliminary analysis for the multinomial logistic regression used in the dissertation began with the univariate and bivariate distributions of the study variables described above. Descriptive statistics, frequency counts, and distributions of all variables were obtained. A correlation matrix was used to examine the bivariate associations between childhood stressors and other continuous variables included in this analysis (the independent variables). The association between COD and the independent variables was assessed using either weighted F test statistics (resulting from Adjusted Wald tests) or regression analysis, depending on the distribution of the independent variable. Frequency histograms and scatterplots were used to

graphically represent and visualize some of the univariate and bivariate associations. The results of the preliminary analyses for the multinomial logistic regression are reported at the beginning of Chapter 4.

3.8.3 Plan for Preliminary Analyses Preceding Survival Analysis

Cox Proportional Hazard Models were the survival analysis method chosen for the research questions in Aim 3. In the preliminary analyses for this Aim, timing of onset of each individual disorder is examined to better understand the onsets of all of the disorders that make up COD and the variation that is in the dependent variable by disorder type. Kaplan-Meier curves for the main categorical predictors were first used to examine the shape of the survival function for each group (i.e. males and females, with and without childhood poverty) and whether groups are proportional (i.e. if the survival functions are approximately parallel across groups) in each of the two samples used in this Aim. Tests of equality of the survival functions for each predictor were used to test whether to include the explanatory variable in the final model, and a significance level of $p<0.05$ was used for this determination. Finally, to conclude preliminary analysis for this Aim, timing is examined at a bivariate level to first determine which disorder (psychiatric or SUD) is more likely to occur first, and the average time between disorder onsets within the population. The results of the preliminary analyses for the Cox Proportional Hazards regression are reported at the beginning of Chapter 6.

3.8.4 Operationalizing Childhood Adversity

Before conducting analyses with the childhood adversity measures, I performed several investigations of the measures of adversities. The questions asked about adversity before age 18 can be seen in Table 3.1 on page 58. The rationale for investigating different measures of childhood adversity for inclusion in the final model is that there is no standard accepted

operationalization of childhood adverse experiences used in psychiatric disorder research, and there is disagreement on the optimal operationalization. Since a summative score has the potential to mask important contributions of specific adversities in understanding COD risk, these analyses sought a measurement approach to childhood adversity that captures the magnitude of exposure to different adversities as well as the frequency of that exposure, and looked for potential potency of particular adverse experiences in determining COD risk.

The childhood adversity investigation involved first analyzing the univariate distributions of each question about adversity, to make decisions about how to construct all 24 childhood stressor questions into a more concise operationalization. I then assess the bivariate associations of each constructed measure with the dependent variable, to determine the strength of the association of each measure with COD. I look at the statistical associations of the adversity measures by using a multinomial logistic regression and post-estimation Adjusted Wald tests. This is done to provide information about how the construction of the adversity measures changes its perceived association with COD.

Ultimately, I examine three operationalizations: 1) a count-based measure of number of adversities (Y/N) that ever occurred (range 0-20, truncated to 15), 2) five separate measures that represent different types of adversities and their frequency (frequency of adverse events in each category: neglect, physical abuse, verbal abuse, sexual abuse, domestic violence, and parental events), and 3) predicted membership in latent classes of adversities. The analyses conducted to determine the optimal measure of adversity to include in the final model can be seen in Chapter 4 beginning on page 111.

3.9 Analytic Plan for Main Analyses

3.9.1 Treatment of Design Effects in NESARC-III

The design effects of NESARC-III require the use of special variance estimation statistical programs for complex survey design that generate the appropriate variance and standard error estimates. In addition, sample weights adjust for differential selection probabilities and nonresponse. The sample weights, strata, and clustering variables that are used to account for the design effects were created by NIAAA and are included in the dataset. Procedures accounting for survey design were used in Stata and MPlus (e.g., the 'svy' command and the 'complex' option, respectively) to develop estimates that account for the design effects of the survey and make these data nationally representative of the adult (18+) non-institutionalized civilian population of the US.

3.9.2 Final Sample Size and Determination of Statistical Significance

The final sample size for Aim 1 and Aim 2 is n = 33,767 once those who are missing data and the American Indians/Alaskan Natives are removed from the analysis. The final sample size for Aim 3 is n = 32,635. The sample size is reduced for Aim 3 compared to Aim 1 and 2 because some respondents did not have an age of onset for COD.

Statistical significance is set at a conservative 0.01 p-value in all multivariate models used to test hypotheses to account for multiple tests conducted for the dissertation.

3.9.3 Analytic Approach for the Multinomial Logistic Regression

The analytic approach is presented according to each Aim of the study and methods of hypothesis testing are discussed below. Multinomial logistic regression was chosen to analyze Aim 1 and 2 because it was the most appropriate given the nominal dependent variable. Multinomial logistic regression is a model that is used to predict the relative risk ratios of the

different possible outcomes of a categorially distributed dependent variable, given a set of independent variables. All of the coefficients produced in this model are relative to a base category and exponentiating the coefficients allows for the generation of relative risk ratios, representing the association of the independent variable with one outcome relative to another. The multinomial logistic regression model can be re-parameterized to produce different comparisons than the ones the model output provides, as I do in the results and tables. The tables for each regression show the models re-parameterized where: in comparison 'A' no disorder is the reference outcome; in comparison 'B' psychiatric disorder only is the reference outcome; and in comparison 'C' SUD only is the reference outcome. Therefore, the RRR's in each table show the relative risk of COD compared to each other disorder outcome.

For the multinomial regression analyses described below, the Adjusted Wald test was used to determine the significance of covariates in the multivariate model; that is, to determine the overall significance of a variable across the four disorder outcomes (i.e. the significance of childhood poverty overall in COD, SUD, and psychiatric disorder compared to no disorder). Occasionally, the Adjusted Wald test was used to test the overall significance of categorical variables that have multiple categories just for a single disorder outcome comparison (i.e. the significance of the four race/ethnicity categories, as a set, in COD compared to no disorder).

3.9.4 Analytic Approach for the Cox Proportional Hazards Regression

For the survival analyses outlined below, bivariate and multivariate associations were estimated using weighted Cox Proportional Hazard Models estimated using the stcox command in Stata 14.0, while survival and hazard curves were generated using the stcurve command in Stata 14.0 (StataCorp, 2016). Post-estimation Adjusted Wald tests were used to determine the significance of groups of categorical variables in the Cox Proportional Hazard models, that is, to

determine the overall significance of categorical variables that have multiple categories (i.e. the significance of the four race/ethnicity categories, as a set, in hazard of COD).

The survival analysis presented in *Section 6.2* uses a nonparametric Cox Proportional Hazard model to avoid making assumptions about the functional form of the survivorship function. I have not found survival analysis done with COD before, so I chose not to constrain the shape of the function apriori. The Cox Proportional Hazard model assumes that the covariates multiplicatively shift the baseline hazard function without assigning a specific survivor function (Cleves, 2008). Because of this flexibility, it is not possible to comment on the absolute risk incurred by a covariate, instead, only the relative hazard of one covariate to another, or of the relative hazard associated with different levels/categories within a variable.

The first set of survival analyses use the whole population and model COD risk over time (relative to all other outcomes together), with the failure in the model being the development of the second disorder. In this time-to-event model that includes the whole sample, someone is at risk for COD from birth until the age they develop COD or until the age at which they are interviewed for NESARC-III. The failure variable in this model is a binary variable that captures lifetime COD (Yes=1/ No=0), and the model accounts for the time between the starting period (birth) and the determination of the outcome. For those who have not yet developed COD by the time they are interviewed, they remain at risk for the entire duration of the study and their observation is censored at the age of interview. Note that this model by design groups together all other outcomes in the "no lifetime COD" group including those with no disorder, those with psychiatric disorder only, and those with SUD only. This is an essential concession because developing a first disorder is a necessary but not sufficient criteria for developing COD, and including a time-varying variable that accounts for the development of a first disorder is too

highly predictive of the outcome of COD, such that including it obscures the relative hazard of other variables. Therefore, COD is operationalized in this model as lifetime COD (accounting for age of onset) relative to all other outcomes.

An alternative method to the Cox Proportional Hazard model would be using a model that considers the development of a single disorder as a failure in addition to considering the development of COD as a failure (the Conditional Risk Set model, for example). Multiple failure models like the Conditional Risk Set model were considered but ultimately were not selected for use in the study because they constrain the effect of covariates to be the same across all failure types. In doing so, they are unable to distinguish the hazard that child poverty, for example, adds to COD relative to SUD. The Conditional Risk Set model would average the effects of child poverty for groups with a single disorder with the effects of childhood poverty for COD, and thus, would not be able to provide information about variables the distinctive hazards associated with COD. Collapsing the single disorder and no disorder individuals into the same category to in the Cox Proportional Hazard model also results in averaging effects across three outcomes together, however, in this case the hazard of COD is observable distinctly from the hazard of all other disorders, and this is a preferable compromise given the focus on COD in this study.

A second set of Cox Proportional Hazard models were estimated, shown in *Section 6.4*, where the analysis was restricted to respondents who had at least one disorder, and was done to determine how risk of COD changes after the development of SUD or a psychiatric disorder. The survival analyses in *Section 6.4* model COD hazard over time (relative to only having a single type of disorder over the life course), with the failure in the model being the development of the second disorder. In this time-to-event model that includes only people who have at least one SUD or psychiatric disorder, someone is at risk for COD from the age they develop any disorder

until the age they have COD or until the age at which they are interviewed. The failure variable in this model is a binary variable that captures lifetime COD (Yes=1/ No=0), and the model accounts for the time between the starting period (age of onset of their first disorder) and the determination of the outcome. For those who have not developed a second type of disorder by the time they are interviewed, they remain at risk for the entire duration of the study and their observation is censored at the age of interview. Not everyone in this sample goes on to develop COD.

3.9.5 Hypothesis Testing for Main Effects

Multinomial logistic regression, which models the log odds of the outcomes as a linear combination of the predictor variables, was first used to model the nominal outcome variable of lifetime COD in Aims 1 and 2. Cox Proportional Hazard models were used to model time of onset of COD as specified in Aim 3. Before this modeling was done, data cleaning and checking, verification of assumptions was performed, as described above in the preliminary analyses.

All hypotheses regarding the association between independent variables and the dependent variable, such as Hypothesis1a1, were tested by using the post-estimation "test" command in Stata 14 following the model estimation. This is true of associations in the multinomial logistic regression models as well as the Cox Proportional Hazard models. The test used in this command is an Adjusted Wald test and the resulting test statistic produced by this command is an F test. This test allows me to reject or fail to reject the null hypothesis, that, for example, childhood poverty is not associated with COD, controlling for other covariates. The decision to reject the null hypothesis is made using the Adjusted Wald test produced by the "test" command that tests, in this example, whether the coefficient for the effect of childhood poverty on COD differs from 0 in a statistically significant way, at the conservative level of $p<0.01$ (a

test of the null hypothesis that H0: $\beta = 0$). Finding a p value larger than 0.01 in this case would lead me to fail to reject the null hypothesis that childhood poverty is not associated with COD.

3.9.6 Hypothesis Testing for Conditional Relationships

To test the hypotheses about the conditional relationships for different racial/ethnic and gender groups, such as Hypothesis1b1, Hypothesis1b2, Hypothesis1c1, and Hypothesis1c2, I created interaction terms that are product variables of the two variables included in the moderation (e.g., gender × child poverty). I then used these interaction terms in models with all other covariates to test the significance of the conditional relationships using the Adjusted Wald test given by the "test" command in Stata 14 to determine if the coefficients for the interaction terms significantly differed from 0 in the model. This is true of the conditional relationships in the multinomial logistic regression models as well as the Cox Proportional Hazard models. For example, with Hypotheses 1c2, I estimate a model that includes the interaction term gender × child poverty to test the null hypothesis (H0: $\beta_{\text{gender} \times \text{child poverty}} = 0$) or that association between childhood poverty and COD is not conditional on gender. The test used in this command is an Adjusted Wald test for the interaction term of gender × child poverty and the resulting test statistic produced by this command is an F test. This test allows me to reject or fail to reject the null hypothesis, based on whether the coefficient for the effect of gender × child poverty differs from 0 in a statistically significant way, at the conservative level of $p<0.01$.

I used the "lincom" command in combination with reversed scoring of categorical variables in Stata to interpret the significant interactions found during the analysis. This command computes point estimates, standard errors, t statistics, p-values, and confidence intervals for linear combinations of coefficients after any estimation command, and it was used

in the interactions to determine the relative risk ratios and hazard ratios for the values of each variable that were not automatically produced in the model output.

For example, when testing the male × child poverty interaction in the example above, the model estimated gives relative risk ratios (RRR) for some but not all of the categorical combinations in the model. Any comparisons desired beyond the comparisons with the reference group, which are in the model output, must be calculated using the lincom command. To test if there is a difference in the relative risk ratio for COD between males with and without poverty, for example, the lincom command can be used to determine the statistical difference of the coefficients of "gender" and "gender × child poverty." To confirm that I obtained correct calculations of the standard errors and p values from the lincom command, I also reversed the scoring for categorical variables in the interactions and obtained the same estimates. In the case of models with multiple significant two-way interactions, I stratified models by one of the terms in one of the interactions to aid in interpretation.

For hypotheses that deal with higher-order interactions, or three-way interactions, such as Hypothesis2b2, Hypothesis2b3, Hypothesis2c2, and Hypothesis2c3, product interaction terms were created with all three variables included in the moderation. The lower-order terms for these interactions were included in the each of the models tested.

For example, for Hypothesis 2b2, that childhood stressors intensifies the association between childhood poverty and COD and that the magnitude of this association differs by race ethnicity, I introduced the following terms into a model with all other covariates: "child adversity count × child poverty × race/ethnicity," " childhood adversity count × child poverty," "race/ethnicity × child poverty," " race/ethnicity × child adversity count," "child poverty," "race/ethnicity" and "child adversity count." The null hypothesis tested in this case is that the

magnitude of the conditional relationship between childhood adversity and childhood poverty is not different across racial/ethnic groups. I either reject or fail to reject this hypothesis based on the test of significance of the "child adversity count × child poverty × race/ethnicity" interaction term using the Adjusted Wald test. This test determines whether or not the co-efficient for the interaction term significantly differ from 0 in the model.

For all three-way interactions tested in this dissertation, I used this procedure to determine if the coefficients for the three-way interaction terms significantly differ from 0 in the model, and if I could subsequently reject or fail to reject these hypotheses. Although no three-way interactions were found, for the purpose of interpreting the three-way interactions in this dissertation, I planned to stratify models by gender or by race/ethnicity to aid in interpretation.

3.9.7 Hypothesis Testing for Relationships in Survival Analyses

To test the hypotheses related to associations of independent variables with the timing of onset of COD, such as Hypothesis 3a and Hypothesis 3b, I follow the same steps outlined in section *3.9.5 Hypothesis Testing with Multivariate Models,* with the only difference being the production of hazard ratios instead of relative risk ratios. For the hypothesis tests with the hazard ratios, I test the null hypothesis that they are equal to 1 and reject the null hypothesis at the $p < 0.01$ level.

For the hypotheses related to moderation of childhood poverty and childhood stressors by racial/ethnic and gender groups, such as Hypothesis 3c1, Hypothesis 3c2, Hypothesis 3d1, and Hypothesis 3d3, I used the same steps outlined in *3.9.6 Hypothesis Testing with Conditional Associations,* again, instead testing the null hypothesis that the hazard ratio for the product interaction terms will equal 1.

3.9.8 Hypothesis Testing with Indirect Associations

Mediation is not formally tested in this dissertation. Due to the dependent variable being categorical, and the data being survey data, testing the hypothesis concerned with mediation, Hypothesis1a2, is not mathematically possible because of the lack of appropriate statistical tests and software that can handle the analysis. The most suitable method for testing mediation would be Structural Equation Modeling, however, this is not currently possible with a nominal outcome and survey data, as it is not possible to estimate the indirect effects. Thus, mediation of the association between childhood poverty and COD by childhood adversity is not formally tested here.

3.9.9 Equations for Estimated Models

Equations for all models in this dissertation can be found in Table 3.3 below. Table 3.3 shows the research questions addressed by each model in the dissertation, and displays the corresponding Aim and model equation for these questions. Rationale for the estimation of each of these equations will be explained in the Main Analyses section below.

The analyses began with the preliminary analyses described above. First are the logistic regressions done to assess whether data are missing at random for those missing on childhood adversity, childhood poverty, and family support, as represented in Models 3.1a, 3.1b, and 3.1c. Each of these logistic regressions assesses demographic differences such as family composition, respondent education, respondent income, gender, race/ethnicity, nativity status, and age between those missing and those not missing data for each of the variables (childhood adversity, childhood poverty, and family support, respectively). These models are separate and do not build on each other but were presented together for space considerations.

Table 3.3 Analysis for Dissertation Research by Research Question

Key:

β_{family} = family composition of childhood home (categorical: 3 dummy variables)

$\beta_{education}$ = respondent's level of education (categorical: 4 dummy variables)

β_{income} = respondent's household income (continuous)

β_{gender} = respondent's gender (categorical)

β_{race} = respondent's race/ethnicity (categorical: 3 dummy variables)

β_{native} = respondent's nativity status

β_{age} = respondent's age (continuous)

$\beta_{Cfsupport}$ = family support < age 18 (categorical)

$\beta_{Cpoverty}$ = childhood poverty <age 18 (categorical)

$\beta_{CSexualAbuse}$ = frequency of childhood sexual abuse (continuous)

$\beta_{CPhysicalAbuse}$ = frequency of childhood physical abuse (continuous)

$\beta_{CVerbalAbuse}$ = frequency of childhood verbal abuse (continuous)

$\beta_{CPhysical/VerbalAbuse}$ = frequency of childhood physical/verbal abuse (continuous)

$\beta_{CNeglect}$ = frequency of childhood neglect (continuous)

$\beta_{CDomesticViolence}$ = frequency of childhood domestic violence (continuous)

$\beta_{CParentalEvents}$ = frequency of childhood parental events(continuous)

$\beta_{Cstress}$ = count of childhood adversities (continuous)

β_{LCA1} = latent class 1 (categorical)

β_{LCA2} = latent class 2 (categorical)

β_{LCA3} = latent class 3 (categorical)

$\beta_{parentSUD}$ = biological mother or father SUD (categorical)

$\beta_{parentMH}$ = biological mother or father psychiatric disorder (categorical)

$\beta_{parentCOD}$ = biological mother or father SUD (categorical)

$\beta_{parentDK}$ = biological mother or father disorder unknown (categorical)

β_{age_first} = age of first substance use (continuous)

β_{psych_first} = respondent has a psychiatric disorder first (categorical)

Aim	Research Question	Statistical Model	Regression Equation
Preliminary Analysis	Are missing data missing at random?	Multivariate logistic regressions (with missing variables as the outcomes)	<u>Model 3.1a (Table 3.1)</u> Missing Childhood Adversity = $\beta 0 + \beta_{family} + \beta_{education} + \beta_{income} + \beta_{gender} + \beta_{race} + \beta_{native} + \beta_{age} + \varepsilon$ <u>Model 3.1b (Table 3.1)</u> Missing Childhood Poverty = $\beta 0+$ (same variables as Model 3.1a) <u>Model 3.1c (Table 3.1)</u> Missing Family Support = $\beta 0+$ (same variables as Model 3.1a)
Preliminary Analysis	What is the optimal classification of childhood adversity variables for this dissertation?	Bivariate Logistic Regression of COD with Childhood Adversity Subgroups	<u>Model 4.1 (Table 4.4)</u> COD = $\beta 0 + \beta_{CSexualAbuse} + \beta_{CPhysicalAbuse} + \beta_{CVerbalAbuse} + \beta_{CNeglect} + \beta_{CDomesticViolence} + \beta_{CParentalEvents} + \varepsilon$
Preliminary Analysis	What is the optimal classification of childhood adversity variables for this dissertation?	Bivariate Logistic Regression of COD Relative to No Disorder, Psychiatric Disorder, and SUD, with LCA Classes	<u>Model 4.2 (Table 4.6)</u> COD = $\beta 0 + \beta_{LCA1} + \beta_{LCA2} + \beta_{LCA3} + \varepsilon$

1	1 a. Are childhood stressors and childhood poverty associated with lifetime occurrence of COD?	Multivariate multinomial logistic regressions (main effects model)	Models 4.3 (Table 4.7) $COD = \beta 0 + \beta_{age} + \beta_{gender} + \beta_{race} + \beta_{native} + \beta_{family} + \beta_{Cfsupport} + \beta_{parentSUD} + \beta_{parentMH} + \beta_{parentCOD} + \beta_{parentDK} + \beta_{age\_first} + \beta_{Cpoverty} + \beta_{Cstress} + \beta_{CSexualAbuse} + \beta_{CPhysical/VerbalAbuse} + \varepsilon$
1	1 c. To what extent does this differ by gender?	Multivariate multinomial logistic regressions (with conditional relationships) Where multiple conditional relationships exist, models are stratified to aid interpretation	Model 5.1a (not tabled) $COD = \beta 0 + (\text{all variables from Model 4.3}) + \beta_{Cstress*gender} + \varepsilon$ Model 5.1b (not tabled) $COD = \beta 0 + (\text{all variables from Model 4.3}) + \beta_{CSexualAbuse*gender} + \varepsilon$ Model 5.1c (not tabled) $COD = \beta 0 + (\text{all variables from Model 4.3}) + \beta_{CPhysical/VerbalAbuse*gender} + \varepsilon$ Model 5.2 (not tabled) $COD = \beta 0 + (\text{all variables from Model 4.3}) + \beta_{Cpoverty*gender} + \varepsilon$ Model 5.3 (Table 5.1) $COD = \beta 0 + (\text{all variables from Model 4.3}) + \beta_{Cstress*gender} + \beta_{Cpoverty*gender} + \varepsilon$ Model 5.4 (Table 5.2) $COD_{male} = \beta 0 + \beta_{age} + \beta_{race} + \beta_{native} + \beta_{family} + \beta_{Cfsupport} + \beta_{parentSUD} + \beta_{parentMH} + \beta_{parentCOD} + \beta_{parentDK} + \beta_{age\_first} + \beta_{Cpoverty} + \beta_{Cstress} + \beta_{CSexualAbuse} + \beta_{CPhysical/VerbalAbuse} + \varepsilon$ Model 5.5 (Table 5.3) $COD_{female} = \beta 0 + \beta_{age} + \beta_{race} + \beta_{native} + \beta_{family} + \beta_{Cfsupport} + \beta_{parentSUD} + \beta_{parentMH} + \beta_{parentCOD} + \beta_{age\_first} + \beta_{Cpoverty} + \beta_{Cstress} + \beta_{CSexualAbuse} + \beta_{CPhysical/VerbalAbuse} + \varepsilon$
1	1 b. To what extent does this differ by racial/ethnic groups?	Multivariate multinomial logistic regressions (with conditional relationships)	Model 5.6a (not tabled) $COD = \beta 0 + (\text{all variables from Model 4.3}) + \beta_{Cstress*} \beta_{race} + \varepsilon$ Model 5.6b (not tabled) $COD = \beta 0 + (\text{all variables from Model 4.3}) + \beta_{CSexualAbuse*} \beta_{race} + \varepsilon$ Model 5.6c (not tabled) $COD = \beta 0 + (\text{all variables from Model 4.3}) + \beta_{CPhysical/VerbalAbuse*} \beta_{race} + \varepsilon$ Model 5.7 (not tabled) $COD = \beta 0 + (\text{all variables from Model 4.3}) + \beta_{Cpoverty*} \beta_{race} + \varepsilon$
2	2.a Does childhood poverty interact with childhood stressors to impact the likelihood of developing COD over the life course?	Multivariate multinomial logistic regressions (with conditional relationships)	Model 5.8a (not tabled) $COD = \beta 0 + (\text{all variables from Model 4.3}) + \beta_{Cstress*Cpoverty} + \varepsilon$ Model 5.8b (not tabled) $COD = \beta 0 + (\text{all variables from Model 4.3}) + \beta_{CSexualAbuse*Cpoverty} + \varepsilon$ Model 5.8c (not tabled)

			COD = $\beta 0+$ (all variables from Model 4.3) $+ \beta_{CPhysical/VerbalAbuse} * Cpoverty + \varepsilon$
2	2.b To what extent do these interactions differ by racial/ethnic groups?	Multivariate multinomial logistic regressions (with conditional relationships)	Model 5.9a (not tabled) COD = $\beta 0+$ (all variables from Model 4.3) $+ \beta_{Cstress} * Cpoverty * race + \beta_{Cstress} * Cpoverty + \beta_{Cpoverty * race} + \beta_{Cstress * race} + \varepsilon$ Model 5.9b (not tabled) COD = $\beta 0+$ (all variables from Model 4.3) $+ \beta_{CSexualAbuse} * Cpoverty * race + \beta_{CSexualAbuse} * Cpoverty + \beta_{Cpoverty * race} + \beta_{CSexualAbuse * race} + \varepsilon$ Model 5.9c (not tabled) COD = $\beta 0+$ (all variables from Model 4.3) $+ \beta_{CPhysical/VerbalAbuse} * Cpoverty * race + \beta_{CPhysical/VerbalAbuse} * Cpoverty + \beta_{Cpoverty * race} + \beta_{CPhysical/VerbalAbuse * race} + \varepsilon$
2	2.c To what extent do these interactions differ by gender?	Multivariate multinomial logistic regressions (with conditional relationships)	Model 5.10a (not tabled) COD = $\beta 0+$ (all variables from Model 4.3) $+ \beta_{Cstress} * Cpoverty * gender + \beta_{Cstress} * Cpoverty + \beta_{Cpoverty * gender} + \beta_{Cstress * gender} + \varepsilon$ Model 5.10b (not tabled) COD = $\beta 0+$ (all variables from Model 4.3) $+ \beta_{CSexualAbuse} * Cpoverty * gender + \beta_{CSexualAbuse} * Cpoverty + \beta_{Cpoverty * gender} + \beta_{CSexualAbuse * gender} + \varepsilon$ Model 5.10c (not tabled) COD = $\beta 0+$ (all variables from Model 4.3) $+ \beta_{CPhysical/VerbalAbuse} * Cpoverty * gender + \beta_{CPhysical/VerbalAbuse} * Cpoverty + \beta_{Cpoverty * gender} + \beta_{CPhysical/VerbalAbuse * gender} + \varepsilon$
3	3.a How does experiencing childhood poverty affect risk of COD onset over time? 3.b Are some types of childhood stressors associated with COD onset over time more strongly compared to others, or to no stressors?	Entire population - cox proportional hazard model with clock starting at birth and time to *second* disorder as the outcome Entire population - cox proportional hazard model with clock starting at birth and time to *second* disorder as the outcome	Model 6.1 (Table 6.3) $\lambda (t_{birth} \mid \text{Second Disorder}) = \lambda_0(t) + \beta_{age} + \beta_{gender} + \beta_{race} + \beta_{native} + \beta_{family} + \beta_{Cfsupport} + \beta_{parentSUD} + \beta_{parentMH} + \beta_{parentCOD} + \beta_{parentDK} + \beta_{Cpoverty} + \beta_{Cstress} + \beta_{CSexualAbuse} + \beta_{CPhysical/VerbalAbuse} + \varepsilon$

3	3.c Does co-occurrence risk change based on which disorder comes first?	Cox proportional hazard model: Just for those who have at least 1 disorder- model clock starting at first disorder and time to *second* disorder as the outcome	Model 6.2 (Table 6.4) $\lambda\ (t_{\text{first disorder}} \mid \text{Second Disorder}) = \lambda_0(t) + \beta_{\text{psych\_first}} + \beta_{\text{age}} + \beta_{\text{gender}} + \beta_{\text{race}} + \beta_{\text{native}} + \beta_{\text{family}} + \beta_{\text{Cfsupport}} + \beta_{\text{parentSUD}} + \beta_{\text{parentMH}} + \beta_{\text{parentCOD}} + \beta_{\text{parentDK}} + \beta_{\text{Cpoverty}} + \beta_{\text{Cstress}} + \beta_{\text{CSexualAbuse}} + \beta_{\text{CPhysical/VerbalAbuse}} + \varepsilon$
3	3.c What is the risk of co-occurrence once a participant develops a psychiatric disorder?	Cox proportional hazard model: Stratified by Psychiatric First Just for those who have at least 1 disorder and have psychiatric first - model clock starting at first disorder and time to *second* disorder as the outcome	Model 6.4 (Table 6.5) $\lambda_{\text{psych\_first}}\ (t_{\text{first disorder}} \mid \text{Second Disorder}) = \lambda_0(t) + \beta_{\text{age}} + \beta_{\text{gender}} + \beta_{\text{race}} + \beta_{\text{native}} + \beta_{\text{family}} + \beta_{\text{Cfsupport}} + \beta_{\text{parentSUD}} + \beta_{\text{parentMH}} + \beta_{\text{parentCOD}} + \beta_{\text{parentDK}} + \beta_{\text{Cpoverty}} + \beta_{\text{Cstress}} + \beta_{\text{CSexualAbuse}} + \beta_{\text{CPhysical/VerbalAbuse}} + \varepsilon$
3	3.d What is the risk of co-occurrence once a participant develops a SUD?	Cox proportional hazard model: Stratified by SUD First Just for those who have at least 1 disorder and have SUD first - model clock starting at first disorder and time to *second* disorder as the outcome	Model 6.5 (Table 6.6) $\lambda_{\text{SUD\_first}}\ (t_{\text{first disorder}} \mid \text{Second Disorder}) = \lambda_0(t) + \beta_{\text{age}} + \beta_{\text{gender}} + \beta_{\text{race}} + \beta_{\text{native}} + \beta_{\text{family}} + \beta_{\text{Cfsupport}} + \beta_{\text{parentSUD}} + \beta_{\text{parentMH}} + \beta_{\text{parentCOD}} + \beta_{\text{parentDK}} + \beta_{\text{Cpoverty}} + \beta_{\text{Cstress}} + \beta_{\text{CSexualAbuse}} + \beta_{\text{CPhysical/VerbalAbuse}} + \varepsilon$
3	3.f To what extent does this risk differ by gender?	Cox proportional hazard models: Just for those who have at least 1 disorder – (testing conditional relationship of gender and disorder sequence)	Model 6.6 (Table 6.4) $\lambda\ (t_{\text{first disorder}} \mid \text{Second Disorder}) = \lambda_0(t) + (\text{all variables in Model 6.2}) + \beta_{\text{psych\_first*gender}} + \varepsilon$
3	3.e To what extent does this risk differ by racial/ethnic group?	Cox proportional hazard models: Just for those who have at least 1 disorder – (testing conditional relationship of race/ethnicity and disorder sequence)	Model 6.7 (not shown) $\lambda\ (t_{\text{first disorder}} \mid \text{Second Disorder}) = \lambda_0(t) + (\text{all variables in Model 6.2}) + \beta_{\text{psych\_first*race}} + \varepsilon$

Further preliminary analyses conducted to determine the associations between different operationalizations of childhood adversity and COD are specified above and shown in Models 4.1 and Model 4.2. Model 4.1 regresses the nominal COD variable on the childhood adversity subgroups: childhood sexual abuse, childhood physical abuse, childhood verbal abuse, childhood neglect, childhood exposure to domestic violence, and parental events in childhood for the purpose of assessing the strength of the associations of different categories of childhood adversity frequency. Model 4.2 regresses COD on the most likely group membership according to the latent class analyses for the three classes of adversity: those exposed to sexual abuse (latent class 1), those exposed to violence (latent class 2), and the low exposure group (latent class 3). Models 4.2 was estimated to determine the associations between the latent classes of exposure to adversity in the population and COD, to determine if the classes of adversity are related to COD outcomes. The subsequent equations for the main analyses will be described in the sections for each Aim below.

3.10 Main Analysis

3.10.1 Aim 1: Determining the Association between Childhood Poverty, Childhood Stressors, and COD

The first Aim of this study was to determine if there is a direct association between childhood poverty, childhood stressors, and COD lifetime occurrence controlling for alternative explanations and possible spuriousness. The research questions and corresponding hypotheses for this Aim were tested using multinomial logistic regression.

Overall Strategy. To begin the analysis for Aim 1, correlations between the independent variables were assessed, this was done to determine the potential for multicollinearity and to determine the spread of responses in each categorical combination of variables. Then, bivariate

associations among the independent variables and COD were assessed to determine the association between each of the demographic variables (race/ethnicity, gender, nativity status, age), the family characteristics (family support, family psychiatric history, family SUD history, and family COD history) and the childhood experience variables (childhood poverty, count of childhood adversity, frequency of sexual abuse, frequency of physical/verbal abuse, age at first substance use) with COD. Then, multivariate analyses for Aim 1 were conducted using all of the variables that had significant bivariate associations with COD and were theoretically important in the development of COD.

COD Regressed on Childhood Poverty, Childhood Adversity, and All Covariates. The first model in the main analysis for this dissertation estimated is shown in the equation for Model 4.3., which is used to test Hypothesis1a1, and Hypothesis1a2. Model 4.3 included the variables childhood poverty, count of childhood adversities, frequency of sexual abuse, frequency of physical/verbal abuse, age of first substance use, family support, family psychiatric history, family SUD history, family COD history, family history unknown, family composition, race/ethnicity, gender, nativity status, and age.

Race/Ethnicity Conditional Effects Models. After the main effects model is estimated in Model 4.3, conditional relationships are introduced into Model 4.3. First, to test Hypothesis1b1 that the relationship between childhood stressors and COD will vary by race/ethnicity, I introduce an interaction between childhood sexual abuse and race/ethnicity into the model. In separate models, I test the significance of a variable that is the product interaction term of childhood verbal/physical abuse × race/ethnicity, and another model that tests the significance of a variable that is the product interaction term of the count of childhood stressors × race/ethnicity.

These three conditional race/ethnicity model equations, that collectively test for differential race/ethnicity effects for childhood adversity, are given in Table 3.3, Model 5.6a-c.

To test Hypothesis1b2, that the relationship between childhood poverty and COD will vary by race/ethnicity, using the same variables as the main effects Model 4.3, I add a variable that is the product interaction term of childhood poverty × race/ethnicity and test its significance: this becomes Model 5.7.

All interactions with multicategory variables like race/ethnicity refer to sets of interaction terms that are tested simultaneously.

Gender Conditional Effects Models. The remaining hypotheses in this Aim are concerned with the variation of the same relationships (childhood poverty with COD and childhood adversity with COD) by gender. For Hypothesis 1c1, as with the race/ethnicity conditional hypotheses, three conditional gender and adversity model equations are created with the introduction of the product interaction terms: childhood verbal/physical abuse × gender, childhood sexual abuse × gender, and childhood stress count × gender. With the exception of the interaction terms, these model equations have the same covariates as Model 4.3, the three new equations can be seen in Model 5.1a-c in Table 3.3. For Hypothesis 1c2, that the relationship between childhood poverty and COD will vary by gender, using the same variables as the main effects Model 4.3, I add a variable that is the product interaction term of childhood poverty × gender and test its significance: this becomes Model 5.2.

Upon finding conditional relationships between childhood stress count × gender and childhood poverty × gender by gender in this Aim, I test whether both conditional relationships remain significant in the same model (Model 5.3) and then, upon finding that they do, I stratify

the analysis for males and for females separately to aid in interpretation (Models 5.4a-c and Models 5.5a-c, respectively).

3.10.2 Aim 2: Testing Moderation of Childhood Poverty and COD by Childhood Stressors

Overall Strategy. The second Aim tested the moderation of childhood poverty by childhood stressors to determine if the effect of childhood poverty on lifetime COD is intensified by the experience of childhood adversities, controlling for alternative explanations and possible spuriousness in the model. After examining if the association of childhood poverty and COD is moderated by childhood adversity, I then look at the extent to which any conditional relationship found differs by race/ethnicity, and then by gender.

Childhood Poverty Conditional on Adversity Models. To begin analyses for Aim 2, I examined the evidence for a conditional relationship between childhood poverty and childhood adversity by testing the statistical significance of the product interaction terms childhood verbal/physical abuse × childhood poverty, childhood sexual abuse × childhood poverty, and childhood stress count × childhood poverty. With the exception of the interaction terms, these model equations have the same covariates as Model 4.3. As with Aim 1, multivariate analyses for Aim 2 were conducted using all of the variables that had significant bivariate associations with COD and were theoretically important in the development of COD. The conditional effects models for childhood poverty and adversity are shown in the equation for Models 5.6a-c. Models 5.6a-c are used to test Hypotheses2a, 2b1, and 2c1.

Third Order Childhood Poverty and Adversity Conditional on Race/Ethnicity Models. To test Hypotheses2b2, that the relationship between childhood poverty and childhood adversity will vary by race/ethnicity, using the same variables as the conditional effects Models 5.6a-c, I add a variable that is the product interaction term of childhood poverty × childhood stress count

× race/ethnicity and test its significance (along with the significance of the lower order terms, such as childhood poverty × childhood stress count): this becomes Model 5.7a. To test Hypotheses2b3, that the relationship between childhood poverty and specific types of childhood adversity will vary by race/ethnicity, using the same variables as the conditional effects Models 5.6a-c, I add a variable that is the product interaction term of childhood poverty × childhood sexual abuse × race/ethnicity and test its significance (along with the significance of the lower order terms, such as childhood poverty × childhood sexual abuse): this becomes Model 5.7b. I repeat this process with the frequency of physical/verbal abuse variable in Model 5.7c.

Third Order Childhood Poverty and Adversity Conditional on Gender Models. The remaining hypotheses in this Aim are concerned with the variation of the same relationships (childhood poverty with childhood adversity) by gender. I repeat the process that I did for the race/ethnicity conditional relationships with the substitution of the race/ethnicity variable for the gender variable, and in doing so, create Models 5.8a-c.

3.10.3 Aim 3: Determining the Association between Childhood Poverty, Childhood Stressors and Time of Onset of COD

Overall Strategy. The third Aim of this dissertation was designed to test the association between experiencing poverty and different types of stress in childhood and the age of onset of lifetime COD, using time-to-event data. The dependent variable for the Aim 3 analyses is the age at which respondents develop their second disorder. For these analyses, the time period studied is the period from birth until someone develops COD, marked by the age at which they have their second type of disorder. The timing of COD in this Aim is estimated through a series of Cox Proportional Hazard models.

Main Effects Model – Whole Sample. Model 6.1 is estimated to test Hypotheses 3a, that

childhood poverty is associated with increased risk of COD over the life course, and to test Hypothesis 3b that childhood stressors are associated with increased risk of COD over the life course. This model tested the associations between the focal independent variable and COD in the entire sample using a Cox Proportional Hazard model with the clock starting at birth and time to second disorder as the outcome, net of other explanations and controlling for covariates. The equation for Model 6.1 can be seen in Table 3.3 and it includes: age, childhood poverty, count of childhood adversity, frequency of sexual abuse, frequency of physical/verbal abuse, family support, family composition, family psychiatric history, family SUD history, family history unknown, family COD history, race/ethnicity, gender, nativity status, and age as covariates. Hypotheses 3a and 3b are evaluated based on the test statistics and corresponding p values in the model for the variables: childhood poverty (H0: $\beta_{\text{childhood poverty}}=0$); and then using a post-estimation Adjusted Wald test for the set of variables childhood adversity count, sexual abuse frequency, and physical/verbal abuse frequency (H0: $\beta_{\text{childhood adversity count}}=0$, $\beta_{\text{sexual abuse}}=0$, & $\beta_{\text{childhood physical/verbal}}=0$) respectively.

Main Effects Model – Sample with Any Disorder. Model 6.1 tested the association between childhood poverty, childhood adversity, and timing of COD onset over the life course (with COD onset being the age at which the second disorder begins) for the entire population. There are additional questions about the development of a second disorder type, after one already has a first disorder type, that cannot be answered within the Cox model from Model 6.1. For example, Hypothesis3c predicts that the rate of co-occurrence given a psychiatric disorder will be greater than it is given the sample has an SUD. To test this hypothesis, Model 6.2 uses an analysis restricted to only those in the sample who develop at least one psychiatric disorder or SUD by the time of interview.

Dropping those with no disorder from the sample, Model 6.2 also used a Cox Proportional Hazard model, but where the clock begins at *first* disorder with time to *second* disorder as the outcome. Here sequence of disorder (SUD first vs. psychiatric disorder first), age, childhood poverty, childhood stressors, family support, family composition, family psychiatric history, family SUD history, family history unknown, family COD history, race/ethnicity, gender, and nativity status were covariates. To be able to reject or fail to reject Hypothesis 3c, I use the t-test statistic and corresponding p value for the coefficient for the disorder sequence variable in Model 6.2, to determine if the hazard ratio differs from 1.

Disorder Sequence Conditional on Gender Model. For Hypothesis 3f, the product interaction term: disorder sequence × gender is introduced into a model with all of the covariates from Model 6.2, this new equation can be seen in Model 6.6 in Table 3.3. Again, this sample is the same Model 6.2, with only those respondents who have one or more disorders in their life time.

Finding a significant conditional relationship between gender and disorder sequence, I stratify the analysis by disorder type and assess time to second type of disorder given SUD as well as time to second type of disorder given psychiatric disorder using two separate Cox Proportional Hazard models. For those who had psychiatric disorder first (including those who only ever had a psychiatric disorder), their time to second disorder (for those who go on to develop one) is estimated using the model equation from Model 6.4 (equation in Table 3.3). Model 6.4 includes all of the variables from Model 6.2 with the exception of the disorder sequence variable, which is newly added to Model 6.4. From this stratified model, it is possible to test Hypothesis 3d, that rate of COD for those who experienced poverty will be greater than it

is for those who did not, using the t-test statistic and corresponding p value for the coefficient for the childhood poverty variable in Model 6.4, to determine if the hazard ratio differs from 1.

For those who had a SUD first (including those who only ever had a SUD), their time to second disorder (for those who go on to develop one) is estimated using the model equation from Model 6.5 (equation in Table 3.3). Model 6.5 includes all same variables as Model 6.2 with the exception of the disorder sequence variable. From this stratified model, it is possible to test Hypothesis 3e, that rate of COD for those who experienced childhood stressors will be great than those who did not, using the t-test statistic and corresponding p value for the coefficients for the childhood adversity count variable, the sexual abuse frequency variable, and the physical/verbal abuse frequency variable in Model 6.5, to determine if any of the hazard ratios differ from 1.

Models 6.2-6.6 test the effect of childhood stressors on timing of second disorder onset for those who already have one disorder and provide additional insight about which specific stressors are associated with onset of the second disorder after a psychiatric disorder or SUD has occurred. Note that models do not always appear consecutively in the text due to the order in which hypotheses were tested and the logical presentation of results.

Disorder Sequence Conditional on Race/Ethnicity Model. Hypotheses 3f and 3g in this Aim are concerned with the variation of the relationship between disorder sequence and risk of COD, by gender, and then by race/ethnicity. For Hypothesis 3g, that the relationship between disorder sequence and COD will vary by race/ethnicity, using the same variables as the main effects Model 6.2, I add a variable that is the product interaction term of disorder sequence × race/ethnicity and test its significance: this becomes Model 6.7. This sample is the same Model 6.2, with only those respondents who have at least one disorder in their life time.

3.11 Chapter Summary

Chapter 3 described the data that are used in this study including the sampling and data collection procedures used in NESARC-III. I introduced the variables used throughout the study and specified how they were operationalized. I described the preliminary analyses for each type of analysis in the dissertation and specified how I determined to reject or fail to reject hypotheses. I go through the analyses for each Aim, referring to the model equations and describing how the specific hypotheses for the study are addressed in each Aim. For the final section in the research design and methodology chapter, I review missing data and identify bias introduced into the study due to violations of the assumption that data are missing at random.

CHAPTER 4:

CHILDHOOD POVERTY, CHILDHOOD ADVERSITY, AND DISORDER

In this Chapter I describe the results of the preliminary analyses as well as the main effects model for Aim 1 analyses outlined in Chapter 3. I first review the weighted sample characteristics. I use Pearson design-based F-tests in weighted cross tabs as well as Adjusted Wald Tests in bivariate regressions to determine the statistical significance of the racial/ethnic and gender differences observed in the demographic characteristics, family characteristics, childhood experiences, and disorders. After presenting the sample characteristics and their variation by gender and race/ethnicity, I describe the three different measurements of childhood adversity examined for this study and show preliminary analyses conducted to determine the optimal operationalization of childhood adversity. I then present the focal relationship between childhood poverty and COD, and the relationship between childhood adversity and COD as determined using a main effects multinomial logistic regression. Throughout the presentation of the results in this dissertation, I compare factors associated with COD relative to each of the other three possible outcomes (no disorder, psychiatric disorder only, and SUD only). By showing the relative risk ratios of COD compared to no disorder, compared to psychiatric disorder only, and compared to SUD only, it becomes apparent which factors are distinctly associated with co-occurrence and which factors are similarly associated with three types of disorder, for example.

4.1 Sample Characteristics

4.1.1 Demographics and Family Characteristics of the Sample

Sample characteristics are used to describe the group under study and will be elaborated here to illustrate who the people in the NESARC-III dataset are, and what characteristics they

possess. I will first describe the demographic characteristics, then the familial circumstances that the respondents grew up in, then I present a description of the childhood experiences that participants had, and finally a summary of the disorders they have experienced throughout their lives. These descriptions will be given first for the whole population, and then variations by gender and race/ethnicity (two status characteristics central to the hypotheses in this study) will be presented.

As seen in Table 4.1, which shows weighted proportions of demographic and family characteristics, the population is roughly balanced in gender, and Non-Hispanic Whites (hereafter: Whites) make up the majority, followed by Hispanics, Non-Hispanic Blacks (hereafter: Blacks), and Non-Hispanic Asian Americans (hereafter: Asian Americans). The majority are born in the US (84.0% overall). Over two-thirds grew up with two biological parents in a nuclear family, and the rest are equally split between being raised in reconstituted step-parent families and single parent families: only 1% of the population grew up in familial configurations other than these three categories.

Family history (either on the biological maternal or paternal side) of psychiatric disorder, SUD, or COD is relatively common, as shown in Table 4.1. Fewer than one in five have a biological mother or father with a substance use problem (in the absence of psychiatric disorder), and fewer than one in five have a parent with a co-occurring substance use and psychiatric disorder. Having a parent with a psychiatric disorder (without SUD accompanying it) is the most common parental disorder: one-third of the sample have a mother or father that meets these diagnostic criteria.

The demographic and family characteristics described here align with the trends seen in the US population insofar as the data are weighted to represent the US population of adult

civilian residents of the US.

Table 4.1 also gives the demographic and family characteristics by gender and racial/ethnic group. F-tests presented in the columns of this table are used to ascertain the presence of overall group differences in the demographic and family characteristics for males compared to females and among racial/ethnic groups. Where indicated based on the presence of a statistically significant F-test statistic, bivariate regressions were used to determine how the racial/ethnic groups varied from each other (i.e. in what direction the differences were, and for which groups, specifically) and how males varied from females. The test statistics from the bivariate regressions are included in the rows below the variables they are testing differences between.

Table 4.1 Demographic and Family Characteristics by Gender and Race/Ethnicity, Proportion or Mean/SD

			Weighted Proportion or Mean/SD							
	Unweighted	Whole sample	Gender			Race/ethnicity				
	N†	Total	Males	Females	ǂ F-test (d.f.)	NH White	NH Black	NH Asian American	Hispanic	ǂ F-test (d.f.)
Characteristic	33,767		n=14,763	n=19,004		n=18,331	n=7,126	n=1,705	n=6,605	
Overall Proportion	33,767	N/A	48.2%	51.8%		67.4%	10.7%	5.7%	14.8%	
Age (years)	33,767	46.140 /17.530	45.510 /17.232	46.720 /17.752		48.330 /18.154	43.070 /16.259	42.720 /16.988	39.880 /15.318	F (2.57, 290.01)= 896.536, p<0.001
Nativity					F (1,113) = 1.934, p=0.167					
US-Born	29,896	84.0%	83.7%	84.4%		95.6%	90.7%	26.3%	47.8%	
*Group differences^*	--	--	--	--		(ref)	t=-6.58, p<0.001	t=-26.81, p<0.001	t=-41.43, p<0.001	
Childhood family structure					F (2.87, 324.71) = 6.113, p<0.001					F (7.69, 869.05)= 115.313, p<0.001
Two biological parents	22,176	70.0%	71.0%	69.1%		72.8%	49.6%	85.9%	67.4%	
*Group differences^*	--	--	(ref)	(ref)		(ref)	(ref)	(ref)	(ref)	
Reconstituted families	6,284	14.2%	13.3%	15.1%		14.3%	18.5%	4.8%	13.5%	
*Group differences^*	--	--	(ref)	t=4.57, p<0.001		(ref)	t=11.65, p<0.001	t=-8.27, p<0.001	t=1.45, p=0.150	
Single parent	6,643	14.7%	14.9%	14.6%		12.0%	30.3%	8.6%	17.8%	
*Group differences^*	--	--	(ref)	t=-0.18, p=0.855		(ref)	t=32.41, p<0.001	t=-4.53, p<0.001	t=12.16, p<0.001	
Other	1,206	1.0%	0.8%	1.2%		0.9%	1.6%	0.6%	1.2%	
*Group differences^*	--	--	(ref)	t=0.93, p=0.352		(ref)	t=4.19, p<0.001	t=-1.34, p=0.182	t=0.59, p=0.558	
Family history					F (1, 113) = 36.823, p<0.001					F (2.93, 331.47) = 32.384, p<0.001

Table 4.1 Demographic and Family Characteristics by Gender and Race/Ethnicity, Proportion or Mean/SD

			Weighted Proportion or Mean/SD							
	Unweighted	Whole sample	Gender			Race/ethnicity				
	N†	Total	Males	Females	ǂ F-test (d.f.)	NH White	NH Black	NH Asian American	Hispanic	ǂ F-test (d.f.)
Characteristic	33,767		n=14,763	n=19,004		n=18,331	n=7,126	n=1,705	n=6,605	
Family history										
Only Co-occurring disorder in family	6,380	17.4%	15.6%	19.1%		19.1%	15.6%	5.2%	15.7%	
*Group differences^*	--	--	(ref)	t=6.60, p<0.001		(ref)	t=-3.88, p<0.001	t=-9.80, p<0.001	t=-4.35, p<0.001	
Family history unknown	2,189	5.0%	5.8%	4.4%	F (1, 113) = 28.847 p<0.001	4.7%	7.1%	7.8%	3.9%	F (2.93, 331.47) = 15.938 p<0.001
*Group differences^*	--	--	(ref)	t=-4.54, p<0.001		(ref)	t=3.87, p<0.001	t=3.12, p=0.002	t=-2.25, p=0.027	
Only psychiatric disorder family history	11,346	33.4%	30.7%	35.9%	F (1, 113) = 43.165 p<0.001	36.5%	25.5%	23.4%	29.0%	F (2.93, 331.47) = 41.389 p<0.001
*Group differences^*	--	--	(ref)	t=7.34, p<0.001		(ref)	t=-9.21, p<0.001	t=-9.73, p<0.001	t=9.13, p<0.001	
Only SUD family history	6,365	16.4%	15.9%	16.9%	F (1, 113) = 14.529 p<0.001	16.1%	19.5%	8.0%	18.6%	F (2.93, 331.47) = 22.708 p<0.001
*Group differences^*	--	--	(ref)	t=1.50 p=0.013		(ref)	t=5.28, p<0.001	t=-5.97, p<0.001	t=3.60, p<0.001	

Note: NA = not applicable, † Analytic *N*, variation is due to item missing data

ǂ The presence overall group variation was assessed with the Pearson design-based F-test

^ The presence of statistically significant differences between race/ethnicity groups and genders was assessed using bivariate regression. Model based t-test statistics and corresponding p values are presented in the row following each variable where group differences were assessed.

4.1.2 Racial/Ethnic and Gender Differences in Demographics and Family Characteristics

Since this dissertation is especially concerned with how early environments impact disorder outcomes later in life, and how these relationships vary by race/ethnicity and gender, I examine variations in demographic and family characteristics that exist in the population here. These foundational variations may set people on trajectories that determine their exposure to childhood poverty and adversity as they grow up.

To determine the presence of racial/ethnic and gender differences in demographic, family, and disorder characteristics, I first conducted Pearson design-based F-tests with weighted crosstabs. These tests determine the presence or absence of overall group differences by race/ethnicity and by gender. Test statistics that determine the significance of these comparisons are presented in the columns labeled F-test within Tables 4.1, 4.2, and 4.3. These tests do not determine directionality or the specific differences between groups (for example, from these tests I am not able to discern if Whites are different from Blacks on nativity status, or which category of family composition is significantly different for males and females). To comment on directionality and specific categorical comparisons, to provide more information about how the groups differ, I conduct bivariate regressions, after the confirmation that significant group differences exist from the Pearson design-based F-tests. All test statistics are presented in Tables 4.1, 4.2, and 4.3, and some are added in text when they are particularly noteworthy.

Although the majority of Americans are born in the US, this varies by race/ethnicity, as would be expected, with relatively few Asian Americans (26.3%) being born in the US, for example. Asian Americans are not the only group more likely to be born abroad: Blacks and Hispanics also have lower proportions of their populations who are US born than Whites. Childhood family structure varies significantly by race/ethnicity, and by gender. Blacks and

Hispanics both have higher proportions of single-parent families than Whites, while Asian Americans have lower proportions. Other family composition characteristics differ by race/ethnicity as well: including the proportion of re-constituted families and other family configurations, as seen in Table 4.1 Although I would not expect to find gender differences in family composition, females are more likely to grow up in reconstituted families than males – a finding that will be elaborated on further in the discussion in Chapter 7.

Family history of psychiatric disorder only, SUD only, or COD only varies by race/ethnicity and by gender. Whites are more likely to have COD and psychiatric disorder in the family than Blacks, Hispanics, and Asians. Hispanics and Blacks are more likely to have SUD in the family than Whites. Females report family history more often than males in the co-occurring and psychiatric disorder categories, but not in the SUD category.

4.1.3 Childhood Social and Material Environment in the Sample

The focal independent variable being considered in this dissertation is childhood poverty and a key independent variable is childhood adversity. These, in addition to the family and demographic characteristics just described, are fundamental elements of exposure to stress in childhood. Before considering the relationship of childhood poverty and childhood adversity with co-occurring substance use and psychiatric disorder, it is important to examine their representation in the population, as Table 4.2 does. Only 15.4% of the population reports living in a family where they received support from government programs aimed to alleviate poverty before age 18, so by this measure nearly one in six people grew up exposed to childhood poverty.

Family support, on the contrary, may alleviate stress in childhood. The family support measure is high in the population, with over 80% of people reporting some kind of support

(answering ‘very often’ to any of the questions that asked about how often they felt someone in the family wanted them to be a success, someone helped them feel important or special, believed in them, etc.).

The majority of people experience at least one childhood adversity before the age of 18 (70.7%). The childhood adversity scores presented in Table 4.2 above are combined scales of the number of events where respondents score 1 for each event that happened more often than “never,” grouped by category. To see the categories of adversity (sexual abuse, verbal abuse, physical abuse, etc.) and the questions included in each category, see Table 3.1 presented in Chapter 3 on page 58.

As the childhood adversity means in the table are difficult to interpret, in terms of what kind of exposure to adversity they represent, I describe the proportions of people exposed/not exposed to each type of adversity in the text instead. This shows the prevalence of each type of adversity in the population, and provides an indication for how widespread these events and circumstances are. In the sexual abuse category, 88.3% of people reported no exposure to any events. For the other categories, a smaller but still substantial proportion reported no exposure to events such as verbal abuse (56.5%), physical abuse (64.5%), and neglect (64.5%). Approximately one in five are exposed to domestic violence events (i.e. violence between male and female adults in their household) before age 18 (27.9%). Parental events such as parental suicide and parental incarceration before age 18 are common experiences given how serious they are: 2 in 5 have at least one such event.

The age at which people use alcohol or drugs for the first time is strongly correlated with psychiatric disorder and SUD outcomes (Heim et al., 2010), with earlier first use of alcohol or drugs increasing likelihood of disorder. In the population, the average age of first use was 21.881

(minimum = 10, standard deviation = 12.882) years old. See a detailed description of the childhood social and material environment in Table 4.2 below.

Table 4.2 gives the childhood experience variables for the whole sample, and then by gender and racial/ethnic group. As with Table 4.1 above, F-tests and indications of group differences from bivariate regression results are presented in this table.

Table 4.2 Childhood Social and Economic Environment Variables by Gender and Race/Ethnicity, Proportion or Mean/SD

	Unweighted		Weighted Proportion or Mean/SD							
		Whole sample	Gender			Race/ethnicity				
	N†	Total	Males	Females	ǂ F-test statistic (d.f.)	NH White	NH Black	NH Asian American	Hispanic	ǂ F-test statistic (d.f.)
Characteristic	33,767		n=14,763	n=19,004		n=18,331	n=7,126	n=1,705	n=6,605	
Childhood Poverty					F(1,113) =5.118,					F (2.76, 312.09) =174.319,
Present	6,921	15.4%	14.9%	15.7%	p=0.026	12.7%	31.3%	6.9%	17.9%	p<0.001
*Group differences^*			--	--		(ref)	t=22.67, p<0.001	t=-4.26, p<0.001	t=6.91, p<0.001	
Childhood Adversity					(N/A)					(N/A)
Early adversity (count, range 0-15)	33,767	3.409 /3.872	3.134 /3.760	3.306 /4.215		3.216 /3.948	3.395 /4.017	2.384 /3.433	3.284 /4.223	
*Group differences^*			(ref)	t=3.52, p=0.001		(ref)	t=2.36, p=0.020	t=-6.32, p<0.001	t=1.36, p=0.177	
Early neglect (count, range 0-4)	33,767	0.650 /1.149	0.702 /1.208	0.602 /1.200		0.623 /1.165	0.618 /1.150	0.628 /1.178	0.768 /1.327	
*Group differences^*			(ref)	t=-6.12, p<0.001		(ref)	t=0.53, p=0.595	t=0.79, p=0.432	t=6.44, p<0.001	
Early physical abuse (count, range 0-2)	33,767	0.521 /0.754	0.549 /0.767	0.494 /0.759		0.535 /0.759	0.539 /0.767	0.427 /0.715	0.481 /0.765	
*Group differences^*			(ref)	t=-5.63, p<0.001		(ref)	t=0.27, p=0.790	t=-4.41, p<0.001	t=-3.18, p=0.002	
Early sexual abuse (count, range 0-4)	33,767	0.251 /0.815	0.128 /0.617	0.367 /1.021		0.251 /0.858	0.313 /0.938	0.127 /0.577	0.256 /0.885	
*Group differences^*			(ref)	t=19.67, p<0.001		(ref)	t=3.50, p=0.001	t=-7.32, p<0.001	t=0.39, p=0.696	
Early verbal abuse (count, range 0-3)	33,767	0.903 /1.158	0.937 /1.174	0.872 /1.163		0.933 /1.118	0.902 /1.115	0.729 /1.111	0.838 /1.170	
*Group differences^*			(ref)	t=-4.10, p<0.001		(ref)	t=-1.16, p=0.249	t=-5.95, p<0.001	t=-3.85, p<0.001	
Early domestic violence exposure (count, range 0-4)	33,767	0.400 /0.960	0.346 /0.926	0.441 /1.063		0.365 /0.939	0.496 /1.087	0.266 /0.832	0.482 /1.096	
*Group differences^*			(ref)	t=7.46, p<0.001		(ref)	t=6.33, p<0.001	t=-3.18, p=0.002	t=6.34, p<0.001	

Table 4.2 Childhood Social and Economic Environment Variables by Gender and Race/Ethnicity, Proportion or Mean/SD

	Unweighted		Weighted Proportion or Mean/SD							
		Whole sample	Gender			Race/ethnicity				
	N†	Total	Males	Females	ǂ F-test statistic (d.f.)	NH White	NH Black	NH Asian American	Hispanic	ǂ F-test statistic (d.f.)
Characteristic	33,767		n=14,763	n=19,004		n=18,331	n=7,126	n=1,705	n=6,605	
Early parental events (count, range 0-7)	33,767	0.550 /0.945	0.506 /0.934	0.591 /1.002		0.562 /0.982	0.595 /0.984	0.250 /0.713	0.543 /0.585	
*Group differences^*			(ref)	t=7.30, p<0.001		(ref)	t=1.77, p=0.080	t=-15.37, p<0.001	t=-0.90, p=0.367	
At least one adverse experience	24,245	69.4%	70.6%	68.2%	F(1,113) =11.530, p=0.005	70.4%	70.8%	61.5%	66.7%	F(2.89, 326.75) =15.687, p<0.001
Family support	28,591	81.1%	81.2%	81.0%	F(1,113)	80.3%	84.9%	83.8%	81.3%	F (2.89, 326.75)
*Group differences^*	--	--	(ref)	t=0.93, p=0.352	=0.116, p=0.735	(ref)	t=4.19, p<0.001	t=-1.34, p=0.182	t=0.59, p=0.558	=11.440, p<0.001
Age of first alcohol/substance use	33,767	21.881 /12.882	19.617 /10.984	23.986 /14.984		21.150 /13.467	22.819 /13.038	27.692 /16.444	22.198 /11.889	
*Group differences^*			(ref)	t=22.31, p<0.001		(ref)	t=4.59, p<0.001	t=13.78, p<0.001	t=3.78, p<0.001	

Note: NA = not applicable, † Analytic *N*, variation is due to item missing data

ǂ The presence overall group variation was assessed with the Pearson design-based F-test

^ The presence of statistically significant differences between race/ethnicity groups and genders was assessed using bivariate regression. Model based t-test statistics and corresponding p values are presented in the row following each variable where group differences were assessed.

4.1.4 Racial/Ethnic and Gender Differences in the Childhood Social and Material Environment

The Theory of Fundamental Causes points to the differences in access to fundamental resources that can be used to promote one's health that vary according to social status. Access to environments that provide resources, or conversely, placement in environments that induce stress happen at different frequencies according to one's racial/ethnic group and according to one's gender: two social statuses under consideration in this study. I present the racial/ethnic and gender differences here in the early environments to show the differential experiences of stress according to these status groups.

Having at least one adversity is more common among males than female and varies by race/ethnicity where 70.4% of Whites, 70.8% of Blacks, 66.7% of Hispanics, and 61.5% of Asian Americans have at least one adverse experience.

Childhood poverty, a challenging situation before the age of 18, also varies by race/ethnicity and gender being more common for females than males and more common for Blacks compared to Hispanics (based on a bivariate logistic regression, $t=22.67$, $p<0.001$) and Blacks compared to Whites (as shown in Table 4.2, $t=6.91$, $p<0.001$). Childhood poverty is less common for Asian Americans than Whites. The differences in prevalence among these groups are dramatic: Blacks for example have a rate of childhood poverty of 31.3%, while Asian Americans have only 6.9%.

Family support can help to buffer the impact of some of these adversities, and indeed, it is present for over 80% of people, but this proportion differs by race/ethnicity (not by gender). Both Blacks and Asian Americans have higher proportions of respondents with family support before the age of 18 than Whites. The gender and race/ethnicity differences reported above are found in Table 4.2.

Age of first substance use varies dramatically by gender: males use substances for the first time much earlier (age 19.617, standard deviation = 10.984, minimum = 10) than females (age 23.986, standard deviation = 14.984, minimum = 10). These mean ages are different by race/ethnicity too: Whites use substance earlier than all other racial/ethnic groups (mean age is 21.150, standard deviation = 13.467, minimum = 10), but are especially early in their substance use, relative to Asian Americans (mean age 27.692, standard deviation = 16.444, minimum = 10).

Bringing these variables together paints a picture of the environments that people grow up in, and how those environments tend to be different depending on one's racial/ethnic group: Whites tend to have higher adversity and lower family support than Blacks and Hispanics, as well as earlier first substance use, but also have lower levels of childhood poverty. Asian Americans seem to fair the best with low levels of adversity, low levels of poverty, high levels of family support relative to other racial/ethnic groups, and higher age of first substance use.

4.1.5 Psychiatric and Substance Use Disorder

Turning from antecedents of disorder to examine the psychiatric and SUD variables for respondents, themselves, Table 4.3 shows that a lifetime disorder with substances in the population is common. One in three people have a diagnosable problem with alcohol or drug use over the course of their lives. Over one in four people have lifetime alcohol use disorder (AUD). AUD is more prevalent in the population than drug use disorders (which happen to one in every ten people).

Other than alcohol, which is responsible for the overwhelming majority of substance use issues, the substances people use in disorders are: marijuana (6.3% lifetime prevalence of disorder), cocaine (2.4% lifetime prevalence), opioids (2.1% lifetime prevalence), stimulants

(1.7% lifetime prevalence), and sedatives (1.1% lifetime prevalence). Less than one percent of the population has disorders with hallucinogens, heroin, solvents, club drugs, or other drugs. The majority of those with SUD only have one SUD in their lifetimes (and as mentioned above, this is usually alcohol use disorder). 75.22% of those with any SUD will have just one disorder, while 24.78% have more than one SUD.

Table 4.3 below shows disorder prevalence in the population and gives the breakdown of this prevalence by gender and by race/ethnicity. As with the previous two tables, F-tests and bivariate regression test statistics are given in this table.

Table 4.3 Psychiatric and Substance Use Disorder Characteristics by Gender and Race/Ethnicity, Proportion

			Weighted Proportion							
		Whole sample	Gender			Race/ethnicity				
Characteristic	Unweighted N† 33,767	Total	Males n=14,763	Females n=19,004	F-test*	NH White n=18,331	NH Black n=7,126	NH Asian American n=1,705	Hispanic n=6,605	F-test*
Own Substance use disorder					F (1,113)= 462.617, p<0.001					F (2.72, 306.94) = 96.856, p<0.001
Alcohol use disorder	10,001	29.2%	36.1%	22.8%		32.6%	22.7%	14.7%	22.6%	
*Group differences^*	--	--	--	--	F (1, 113) = 140.449, p<0.001	(ref)	t=-9.75 p<0.001	t=-10.19 p<0.001	t=-11.76 p<0.001	F (2.72, 306.94) = 23.580, p<0.001
Other drug use disorder	3,548	9.9%	12.4%	7.5%		10.8%	9.8%	3.8%	7.2%	
*Group differences^*	--	--	--	--		(ref)	t=-0.99, p=0.323	t=-6.38, p<0.001,	t=-5.22, p < 0.001	
Own Psychiatric disorder					F (1,113)= 428.435, p<0.001					F (2.94, 332.27)= 100.046, p<0.001
Internalizing disorder	11,524	31.8%	24.7%	38.4%		35.3%	25.5%	17.6%	25.1%	
*Group differences^*	--	--	--	--		(ref)	t=-9.59 p < 0.001	t= -11.71 p < 0.001	t= -10.89 p < 0.001	
Externalizing disorder	1,754	4.7%	6.8%	2.7%	F (1, 113)= 247.561 p<0.001	4.6%	5.6%	2.7%	4.4%	F (2.93, 330.96) = 8.241, p<0.001
*Group differences^*	--	--	--	--		(ref)	t=2.91, p = 0.004	t= -3.55 p < 0.001	t= -0.45 p =0.656	
Post-traumatic stress disorder	2,339	6.1%	4.2%	7.9%	F (1, 113)= 115.761 p<0.001	6.4%	6.3%	2.1%	5.4%	F (2.81, 317.15) = 12.208, p<0.001
*Group differences^*	--	--	--	--		(ref)	t=-1.94, p=0.055	t=-4.89, p<0.001	t=0.14 p=0.889	
Personality disorder	5,010	13.1%	14.3%	12.0%	F (1, 113)= 24.805 p<0.001	13.5%	14.1%	6.1%	12.0%	F (2.96, 334.14) = 18.800 p<0.001
*Group differences^*	--	--	--	--		(ref)	t=1.19, p=0.238	t=-6.53, p<0.001	t=-1.87 p=0.064	
Eating disorder	617	1.8%	0.8%	2.7%	F (1, 113)= 107.382 p<0.001	2.0%	1.0%	1.3%	1.4%	F (2.93, 331.57) = 6.213 p<0.001
*Group differences^*	--	--	--	--		(ref)	t=-3.89 p<0.001	t=-1.60, p<0.113	t=-2.03, p=0.044	

Table 4.3 Psychiatric and Substance Use Disorder Characteristics by Gender and Race/Ethnicity, Proportion

			Weighted Proportion							
		Whole sample	Gender			Race/ethnicity				
	Unweighted N†	Total	Males	Females	F-test*	NH White	NH Black	NH Asian American	Hispanic	F-test*
Characteristic	33,767		n=14,763	n=19,004		n=18,331	n=7,126	n=1,705	n=6,605	
Own Co-occurring disorder					F (2.84, 321.38)= 325.837					F (7.24, 818.39) = 56.819
No disorder	18,066	48.9%	48.2%	49.5%	p<0.001	44.3%	55.8%	68.3%	58.5%	p<0.001
*Group differences^*	--	--	(ref)	(ref)		(ref)	(ref)	(ref)	(ref)	
Co-occurring disorder	6,158	17.2%	18.0%	16.4%		19.2%	13.6%	5.9%	13.4%	
*Group differences^*	--	--	(ref)	t=-2.99, p=0.003		(ref)	t=-8.15, p < 0.001	t=-12.48, p<0.001	t=-10.21, p<0.001	
Psychiatric disorder only	7,313	19.6%	13.0%	25.6%		20.7%	18.3%	15.7%	16.9%	
*Group differences^*			(ref)	t=17.86, p<0.001		(ref)	t=-5.67, p < 0.001	t=-8.08, p<0.001	t=-9.39, p<0.001	
Substance use disorder only	4,772	14.4%	20.9%	8.5%		15.8%	12.4%	10.1%	11.3%	
*Group differences^*			(ref)	t=-22.87, p<0.001		(ref)	t=-6.97, p < 0.001	t=-7.23, p<0.001	t=-11.27, p<0.001	

Note: NA = not applicable, † Analytic *N*, variation is due to item missing data

ǂ The presence overall group variation was assessed with the Pearson design-based F-test

^ The presence of statistically significant differences between race/ethnicity groups and genders was assessed using bivariate regression. Model based t-test statistics and corresponding p values are presented in the row following each variable where group differences were assessed.

Lifetime psychiatric disorders also exist commonly: 36.7% of the population develops a psychiatric disorder during their lives. The categories of disorders that make up this measure are, internalizing disorders (including major depressive disorder, dysthymia, panic disorder, generalized anxiety disorder, social phobia, specific phobia, agoraphobia, mania, bipolar disorder), personality disorders (schizotypal personality disorder and borderline personality disorder), post-traumatic stress disorder (including only post-traumatic stress disorder), externalizing disorders (conduct and antisocial personality disorder), and eating disorders (bulimia and anorexia).

Internalizing disorders make up the largest proportion of psychiatric disorders that people develop, as seen in Table 4.3) with major depressive disorder being by far the most common individual disorder (20.48% lifetime prevalence in the whole population). The second most common disorder is borderline personality disorder (9.48% lifetime prevalence). Generalized anxiety is next in terms of prevalence of disorder (7.65%), followed by dysthymia (5.48%), post-traumatic stress disorder (5.95%), and conduct disorder (4.61%). Other disorders occurred rarely in the population. Often, people have more than one disorder of the same type. Among those who have a psychiatric disorder, it is more common to have more than one psychiatric disorder than only one disorder. 44.78% of those with any psychiatric disorder only have one, while 55.22% have more than one psychiatric disorder (results not tabled).

The measure of COD, the dependent variable, combines the separate measures of lifetime psychiatric and substance disorders. Overall, half of the population has no lifetime disorder of any type, while one in five have a psychiatric disorder only, nearly one in five have co-occurring substance and psychiatric disorders (meaning that over their lifetimes they will have at least one of each type of disorder), and just under 15% have SUD only. As demonstrated with this

variable, COD is highly prevalent in the population: a serious problem given how severe the condition can be.

4.1.6 Racial/Ethnic and Gender Differences in Psychiatric and Substance Use Disorder

It is well-known that the prevalence of disorder varies by race/ethnicity and gender, a phenomenon highlighted in the literature review for this dissertation. Still, it is important to study the variability by race/ethnicity and gender in this sample, to understand how the dependent variable changes by these status characteristics. In terms of disorders with any substance, this happens more frequently for men than women, and for Whites than their Black, Hispanic, and Asian American counterparts. AUD is not evenly distributed across race/ethnicity and gender groups. Men are more likely to have AUD than women (36.1% vs. 22.8%) and Whites (32.6%) are more likely to have lifetime AUD than their Black (22.7%), Hispanic (22.6%), and Asian American (14.7%) counterparts. Lifetime disorders with drugs other than alcohol are also more common among men than women (12.4% vs. 7.5%), and among Whites (10.8%) than those who are Hispanic (7.2%) or Asian American (3.8%) but not Blacks (9.8%).

Psychiatric disorders are more common for females than males and more common for Whites than all other racial/ethnic groups. The internalizing and eating disorders seen in Table 4.3 follow the trends described above by race/ethnicity and gender, however, externalizing disorders are more common for Blacks than Whites, Hispanics, or Asian Americans (based on a bivariate logistic regression: for externalizing disorder with Blacks as the reference group $t=2.91$, $p = 0.004$, $t=2.75$, $p<0.001$, $t=4.72$, $p=0.007$, respectively), personality disorders are more common for Blacks than Asian Americans (based on a bivariate logistic regression: for personality disorders with Blacks as the reference group $t=6.60$, $p<0.001$), and for post-traumatic stress disorder, the only discernable difference in rates is between Whites and Asian Americans,

where Asian Americans are less likely to have the disorder (test statistics demonstrating these relationships are shown in Table 4.3).

The dependent variable, the categorical measure of COD with other disorder outcomes, is important to examine by race/ethnicity and gender as well, given the variations in the disorders described above and the centrality of this measure in the study. SUD prevalence is markedly different by gender with the most striking differences being males who are more likely to have SUD only (20.9% vs. 8.5%) and females who are more likely to have psychiatric disorder only (25.6% vs. 13.0%). Racial/ethnic differences exist as well. The lowest rates of all disorders (COD, SUD, psychiatric) and the highest rate of no disorder are seen in the Asian American population. Whites more often have a disorder than not, with approximately 20% of Whites belonging to each of the COD and psychiatric only groups and close to 15% with SUD only. Blacks, Asian Americans, and Hispanics are all less likely to have co-occurring, substance use, and psychiatric disorder than Whites.

4.2 The Measurement of Childhood Adversity

Before conducting analyses with the childhood adversity measures, I performed several investigations of the measurement of adversities to come up with the optimal operationalization of the construct for this study. I first describe the three possible operationalizations under consideration: 1) a count-based measure of number of adversities (Y/N) that ever occurred, 2) five separate measures that represent different types of adversities and their frequency, and 3) a latent class analysis of the adversities. Then, I assess the relation of the variables constructed for each operationalization with other variables, including the dependent variable (COD). This last

step enables detection of how the various ways of categorizing childhood adversity impact the assessment of its relationship with COD.

4.2.1 Three Potential Ways to Categorize Childhood Adversity

Respondents are asked about childhood stressors in a set of twenty-four questions asking about experiences before age 18 and include questions about how the caregiver/ household member treated the respondent, questions about how other adults treated them, and questions about experiences that happened to any other adult living in the home. The questions for this section can be seen in Table 3.1. The caregiver questions include eighteen items that ask about sexual abuse, verbal abuse, physical abuse, neglect, and domestic violence. The questionnaire asks about how often these experiences happened on a scale from 0 ("never") to 4 ("very often"). The other six questions ask about experiences that happened to any adult in their household before the child was 18 including imprisonment, alcohol or drug use causing problems, hospitalization for psychiatric disorder, and suicide attempts and outcomes.

There is uncertainty regarding the best way to capture measures of childhood adverse events in psychological disorder research (Schilling et al., 2009), and therefore I examined different ways of categorizing adversity below and how various measures correlate with COD, before selecting the final variables for use. The reasons for examining each adversity measure are as follows:

1) <u>For the count-based measure:</u> Summing the number of adverse experiences that ever happened before 18 is the most common operationalization of adversity used in existing research, and it has the benefit of simplicity and sufficient variation in response as indicated by a wide range of values;

2) For the frequency by type measure: Grouping the frequency of stressors by "types" of events/circumstances (including physical abuse, verbal abuse, sexual abuse, neglect, domestic violence, and parental events), adds information that might be valuable in terms of associated risk of COD, namely, how often the adversities within each category happened. It loses the simplicity of a single measure, but allows for detection of relationships between specific types of events and COD; and
3) For the latent classes: Conducting a latent class analysis can detect the presence of unmeasured classes of adverse experiences in the population that cluster together for groups of people. This approach may pick up associations between types of adversities that are not seen in the other two operationalizations, and this operationalization is not constrained by my own pre-conceived choices of how to group adversities.

4.2.2 Count-Based Measure of Childhood Adversity

The count-based measure of all possible childhood adversities, where any occurrence of the adversity in each question scores a '1' in the count, has a range of 0-20, however, based on the fewer than 5% of the sample that scored over 15 on this measure, it is truncated to 15. The variable has a left-skew with 30.64% of the population reporting no adverse events. The proportion of the population with only 1 adversity is 16.64%, and 2 adversities happen for 10.51% of the population. The proportion of people decreases with each additional adversity in the count. The distribution of this measure in the population and its components (number of physical abuse, verbal abuse, sexual abuse, neglect, domestic violence, and parental events, etc.) is described in the *Sample Characteristics* section above and these values can be seen on page 93.

4.2.3 Association between the Count-Based Measure of Childhood Adversity and COD

It is important to understand how the various ways of measuring adversity affect the conclusions drawn about the association between adverse childhood experiences and COD in this study. The associations between the count of childhood adversities and COD relative to all three comparisons are also significant, although the magnitude of the associations are small, when all other covariates (age, race/ethnicity, gender, nativity, family composition, family support, family history, age of first substance use, and childhood poverty) are added to the model. Here, the childhood adversity count has a relative risk of 1.181 compared to no disorder (based on a multivariate multinomial logistic regression: RRR= 1.181, t=26.41, $p < 0.001$), 1.053 (t=6.81, $p < 0.001$) compared to psychiatric disorder, and 1.132 (t=18.73, $p<0.001$) compared to SUD (model not shown).

4.2.4. Frequency Measure of Types of Childhood Adversity

Adversities were divided into categories to represent the types of events that happened in childhood. Six categories were created based on the nature of questions in the variables: sexual abuse, physical abuse, verbal abuse, domestic abuse, neglect, and parental events. Frequencies were reported on a scale of 0-4 where 0 represented “never” and 4 represented “very often.” Frequency of events within each category of adversity was calculated by taking the average of the responses reported for each of the variables within the category to produce six continuous variables that represented how often the events for that category happened. Parental events were the exception to this because they were asked as ‘yes/no’ rather than how often they happened. The parental events were summed as a count variable (range 0-7).

All six frequency variables were left skewed, with a wide range in the extent of the skew. The frequency of responses at ‘0’ ranged from 56.3% (verbal abuse) to 88.1% (sexual abuse),

when weighted, meaning the events in that category never happened. Mean frequency of sexual abuse was the lowest of the variables at 0.121 (SD 0.491). Domestic violence also had a relatively low frequency in the population on average (mean 0.200, SD 0.617), as did neglect (0.243, SD 0.528). Physical abuse had a frequency of 0.461 (SD 0.847). Frequency of verbal abuse was the highest in the population at 0.559 (SD 0.897). Parental events had a mean count of 0.553 (SD 0.970).

4.2.5. Association between Frequency Measure of Types of Childhood Adversity and COD

Significant associations are also seen with some of the frequency measures of childhood adversity and COD relative to no disorder. Table 4.4 (Model 4.1) shows the results of a multivariate multinomial logistic regression conducted with disorder outcomes regressed on the six variables of the frequency of adversity and all other covariates. Results of Model 4.1 are discussed below.

Table 4.4 Multinomial Logistic Regression of COD Outcomes on Types of Childhood Adversity

	Model 4.1: Co-occurring Disorder Relative to								
	A: No Disorder			B: Psychiatric Disorder Only			C: Substance Use Disorder Only		
Characteristic	RRR		S.E.	RRR		S.E.	RRR		S.E.
Childhood Adversity (frequency)									
Early sexual abuse	1.780	***	0.127	1.061		0.050	1.597	***	0.117
Early physical abuse	1.135	**	0.044	1.016		0.045	1.063		0.053
Early verbal abuse	1.533	***	0.068	1.166	ǂ	0.052	1.282	***	0.054
Early neglect	1.147		0.071	0.987		0.050	1.229	***	0.071
Early domestic violence exposure	0.917		0.041	0.934		0.040	1.026		0.057
Early parental events (count)	1.140	***	0.030	1.028		0.023	1.133	***	0.032
Model Statistics: Design df = 113, F (78,36) = 95.59, p <0.001									

Note: Model is estimated with each comparison relative to COD as the reference group, RRR are re-parameterized to show COD relative to the comparison outcome, model controls for age, gender, race/ethnicity, nativity status, childhood family composition, family history variables, family support, childhood poverty, and age at first substance use.
SE = robust standard error, RRR = relative risk ratio, / = omitted reference category
ǂ p<.05; ** p<.01; *** p<.001, Analytic significance level is set to p=0.01 to account for multiple comparisons

When all types of events are considered simultaneously, sexual abuse frequency was positively associated with COD relative to no disorder and SUD only, but not relative to psychiatric disorder only. Next, physical abuse frequency had a 1.135 risk ratio for COD relative to no disorder but added no significant increase in risk compared to those who had any other kind of disorder. For the verbal abuse category, each increase in frequency was associated with a 53.3% increase in risk of COD relative to no disorder, and a 28.2% increase relative to SUD.

Turning from overt acts of abuse to acts of neglect, frequency of neglect was associated with a 22.9% increase in risk of COD relative to SUD but not relative to other outcomes, net of all other covariates. Last, number of parental events was associated with COD risk relative to both no disorder and SUD, with risk ratios of 1.140 ($t=4.92$, $p<0.001$) and 1.133 ($t=5.41$, $p<0.001$), respectively.

Looking across all contrasts, some patterns emerge: no one type of adversity is significant across all contrasts, domestic abuse is non-significant in all comparisons, sexual abuse and parental events are significantly positively associated with both COD relative to no disorder and SUD. Frequency of adversity did not differentiate risk for COD compared to psychiatric disorder for any of the adversity categories examined, net of all other types of events and controls.

4.2.6. Latent Class Analysis with Childhood Adversity

A latent class analysis was conducted to identify potential unmeasured class membership for the childhood adversity variables. This was done to detect different classes of exposure to adversity before the age of 18, to assess the potential that discrete adverse experiences are clustered or patterned in the population according to underlying latent variables.

There were 18 childhood adversity variables treated as continuous in the model (the abuse, neglect, and domestic violence events) and six categorical (present/absent) variables in the

model (the parental events). A latent class analysis was performed with 20 random starts and the best loglikelihood value (-577643.725) was replicated at least twice. Variables adjusting for complex survey design and sample weights were added the model.

Based on the results of other studies that performed latent class analysis for adversities (Cavanaugh et al., 2015), models containing both three and four latent classes were tested. Due to the small sample size in two of the classes in the model with four classes, the three-class option was preferred. The Vuong-Lu-Mendell-Rubin likelihood ratio test for two versus three classes was performed and three classes were preferred (H0 Loglikelihood Value = -627333.648, $p>0.05$).

The proportions of respondents in each of the three classes are model-based whereas membership in a class is a prediction of the model, meaning that membership is not an ascertained or fixed characteristic, rather the class people are put in reflects the group they most likely belong to based on the prediction of the model. Three classes were obtained with n=1,300 (3.04%), n=4453 (11.89%), and n=30,440 (84.75%) individuals in each based on most likely latent class membership as determined by the conditional response probabilities.

The three latent classes that emerged can be described, generally, as 1) Class 1: those exposed to sexual abuse, 2) Class 2: those exposed to violence, and 3) Class 3: low-exposure individuals. The latent classes are characterized based on the means and probabilities seen in Table 4.5 and depicted in Figures 4.1a-c and 4.2. The figures show the average values for each of the variables included in the model, by latent class. Looking at how the mean values vary based on latent class membership provides a way of understanding how the classes of people are different from each other.

Table 4.5 shows the mean values and probabilities with their corresponding standard errors for all the adversity variables by classes. To see the exact text for each adversity variable, refer to Table 3.1.

Table 4.5 Predicted Means and Probabilities of Childhood Adversity Variables based on Predicted Latent Class Membership

	Predicted Membership in Latent Class 1 "Exposed to Sexual Abuse" (n=1,300, 3.04%)		Predicted Membership in Latent Class 2 "Exposed to Violence" (n=4,453, 11.89%)		Predicted Membership in Latent Class 3 "Low Exposure Individuals" (n=30,440, 84.75%)	
Variable	Mean/ Probability	SE	Mean/ Probability	SE	Mean/ Probability	SE
Neglect1 (Dangerous chores)	1.362	0.067	1.156	0.034	0.222	0.006
Neglect2 (Left alone)	1.427	0.059	1.318	0.044	0.254	0.007
Neglect3 (Deprived of essentials)	1.003	0.066	0.855	0.039	0.083	0.003
Neglect4 (Went hungry)	0.779	0.056	0.617	0.033	0.035	0.002
Neglect5 (No medical attention)	0.834	0.050	0.579	0.023	0.038	0.002
Verbal Abuse1 (Parent insult)	2.109	0.085	2.372	0.033	0.359	0.011
Verbal Abuse2 (Parent threaten)	1.618	0.072	2.046	0.028	0.324	0.011
Verbal Abuse3 (Feared parent hurt)	1.881	0.080	2.158	0.037	0.185	0.009
Physical Abuse1 (Parent hit)	1.912	0.072	2.178	0.032	0.347	0.013
Physical Abuse2 (Parent injured)	1.528	0.068	1.623	0.039	0.092	0.006
Sexual Abuse1 (Adult touch)	2.617	0.062	0.313	0.025	0.068	0.003
Sexual Abuse2 (Touch adult)	2.209	0.065	0.160	0.016	0.035	0.002
Sexual Abuse3 (Attempt intercourse)	2.486	0.049	0.126	0.009	0.024	0.002
Sexual Abuse4 (Have intercourse)	2.077	0.079	0.065	0.006	0.016	0.002
Domestic Violence1 (Male pushed)	1.325	0.099	1.548	0.069	0.131	0.005
Domestic Violence2 (Male kicked)	1.135	0.100	1.187	0.068	0.056	0.003
Domestic Violence3 (Male repeatedly hit)	0.962	0.083	0.918	0.062	0.031	0.002
Domestic Violence4 (Male threaten knife/gun)	0.529	0.047	0.390	0.030	0.014	0.001
Parental Drinking (/No)	55.0%	0.026	57.4%	0.015	17.5%	0.004
Parental Drugs (/No)	23.3%	0.017	18.6%	0.009	3.4%	0.002
Parental Incarceration (/No)	27.9%	0.018	25.7%	0.011	4.5%	0.002
Parental Psych Hospitalization (/No)	18.6%	0.017	14.2%	0.008	3.7%	0.001
Parental Suicide Attempt (/No)	16.8%	0.016	10.4%	0.007	1.7%	0.001
Parental Suicide Success (/No)	3.9%	0.007	1.8%	0.002	0.7%	0.001

Note: SE = robust standard error

Figure 4.1a, 4.1b, and 4.1c show graphs of the means for each latent class, grouped by type of adversity. Figure 4.2 shows a graph of the probability of each categorical adversity event for each latent class.

Figure 4.1a Latent Class Analysis Results – Neglect Variables

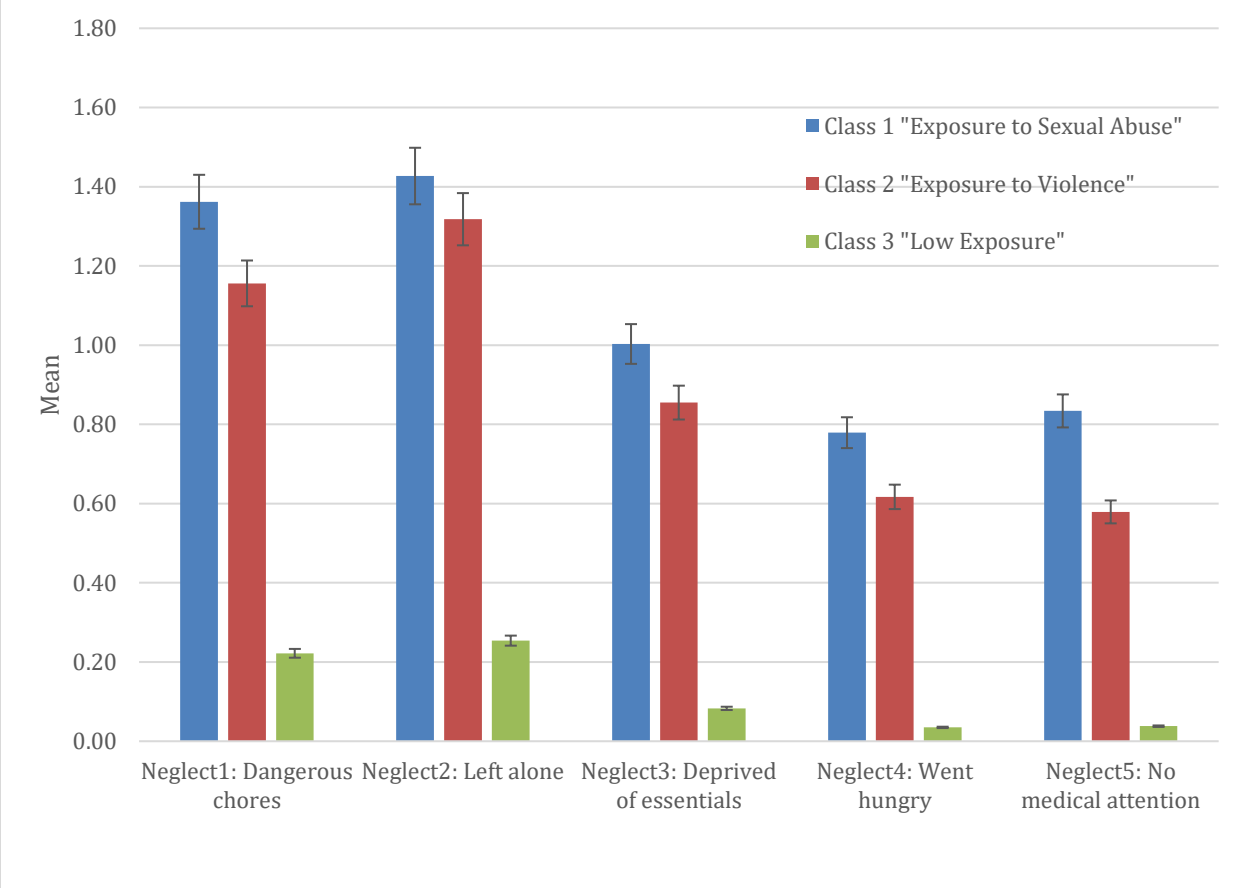


Figure 4.1b Latent Class Analysis Results – Domestic Violence Variables

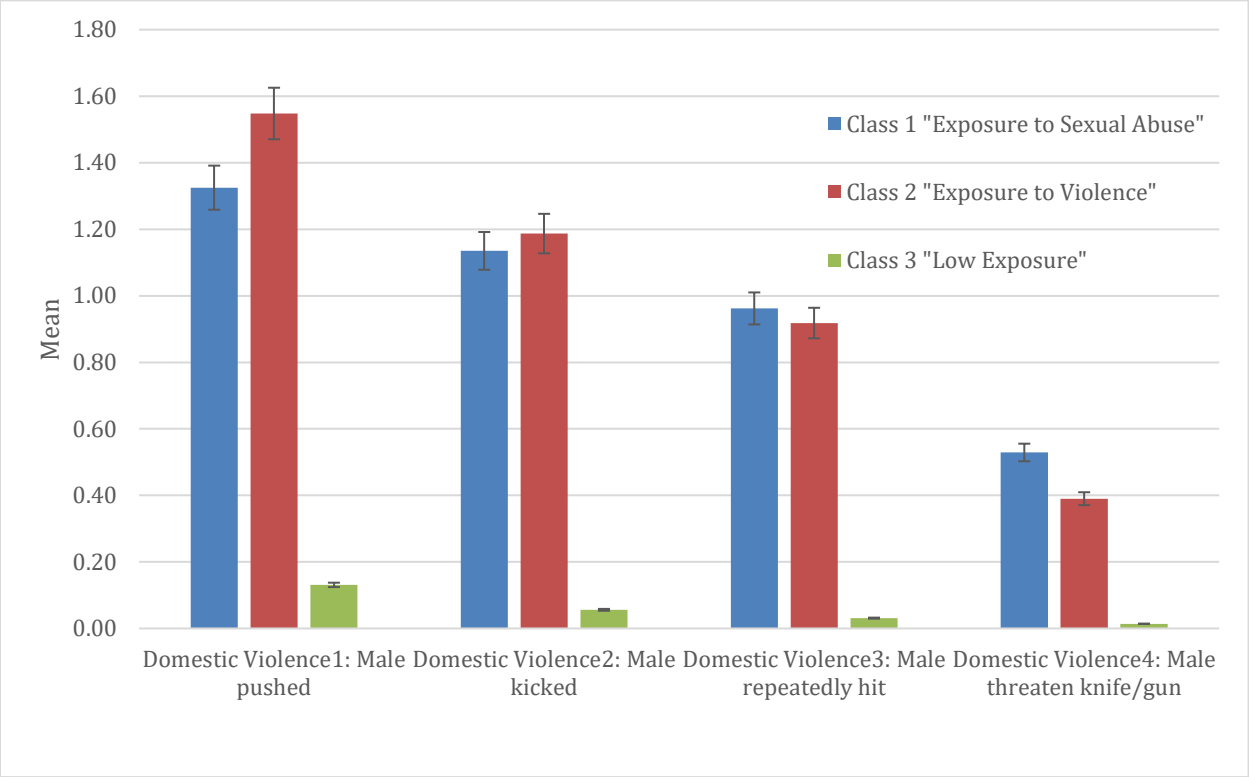


Figure 4.1c Latent Class Analysis Results – Abuse Variables

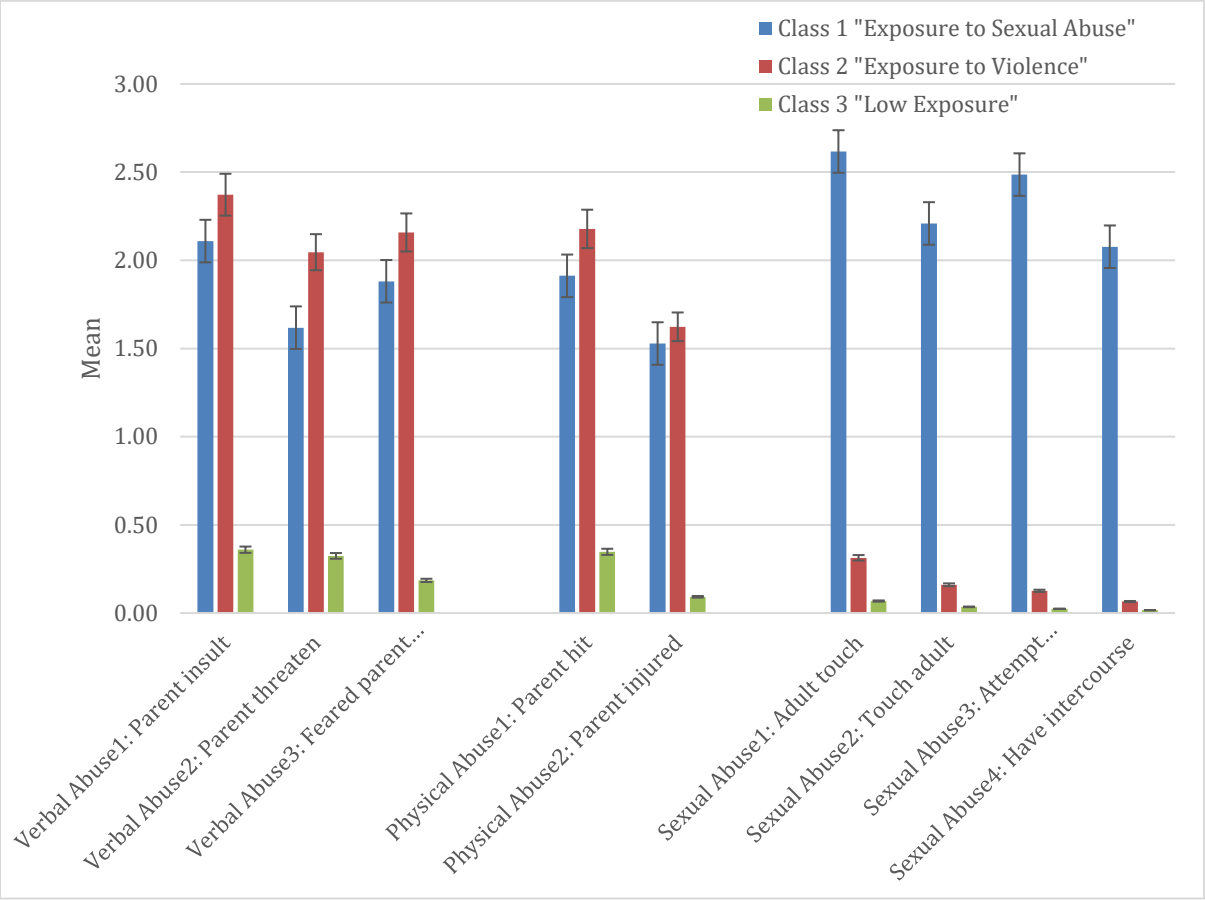
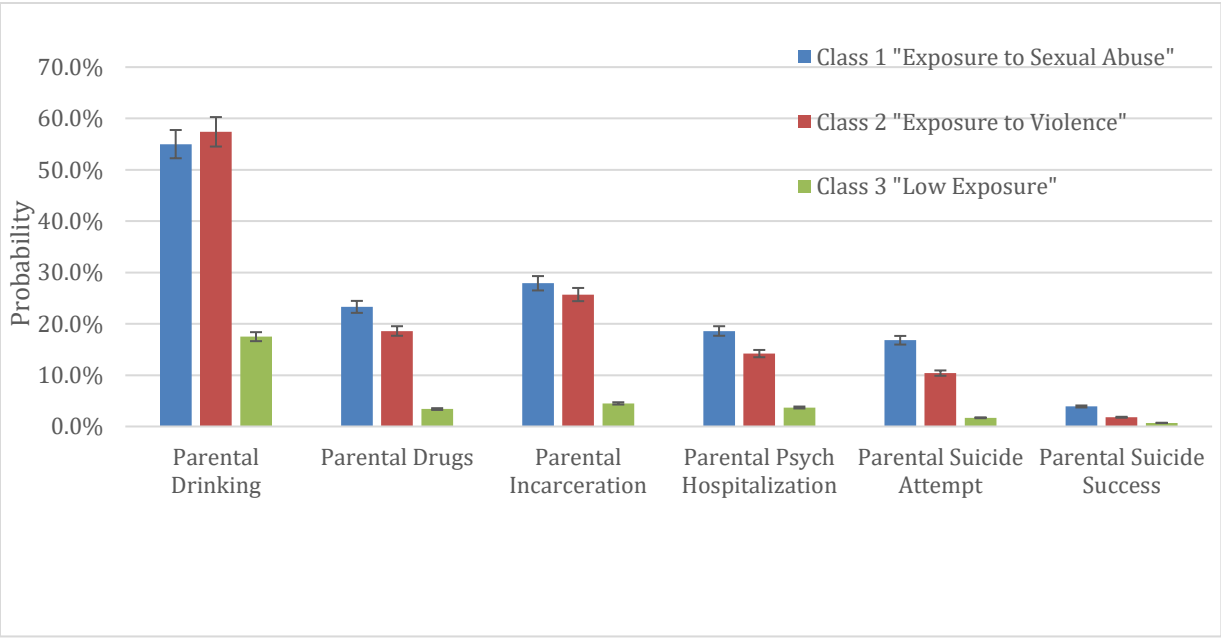


Figure 4.2 Latent Class Analysis Results –Parental Event Variables



Latent Class 1, labeled, those "exposed to sexual abuse" had the highest mean values for the neglect variables, and also had substantially higher sexual abuse values than the other two classes, as seen in Figure 4.1. Physical, verbal, and domestic abuse values for this group were lower than they were for those in the "exposed to violence" group (latent class 2) but markedly higher than the "low exposure" group (latent class 3). Respondents in the "exposed to sexual abuse" category experience high levels of abuse overall, and have the highest probabilities of parental events (except for parental alcohol abuse) compared to all other classes. They have more than a one in four probability of having at least one parent incarcerated and similar chance of having a parent with drug abuse problems before age 18: a trend visible in Figure 4.2.

Latent Class 2, "those exposed to violence" scored the highest means in verbal abuse, physical abuse, and domestic violence measures, but scored low on sexual abuse variables and moderately on neglect variables. This group has the highest probability (nearly 60%) of having parental alcohol abuse and also has relatively high probabilities of the other parental events (especially when compared to the low exposure individuals).

Latent Class 3, the "low-exposure" individuals, was the largest group and had low means on the abuse, neglect, and domestic violence variables and low probabilities of parental events. Probability of parental alcohol abuse for this group was less than one in five.

4.2.7. The Association of the Latent Classes with Childhood Adversity and COD

Model 4.2 in Table 4.6 shows the results of a multivariate multinomial logistic regression where the COD outcome was regressed on the three latent classes, along with all other covariates. Table 4.6 displays the RRRs, the SE and the level of statistical significance (where present) for each of the variables in the multivariate multinomial logistic regression model. The values displayed in Model 4.2 are all derived from the same multinomial logistic regression, they

simply show the risk ratios for lifetime COD relative to the other three outcomes (no disorder, psychiatric disorder only, and SUD only).

Those exposed to sexual abuse (where the low exposure group was the reference) were much more likely to have COD than no disorder (RRR = 4.836, t=12.02, p<0.001), and while those exposed to violence (compared to the low exposure group) also had a higher relative risk of COD compared to no disorder (RRR=2.592, t=16.54, p<0.001 respectively), the difference was not as pronounced as it was for those exposed to sexual abuse.

Those exposed to sexual abuse and exposed to violence were both more likely to have COD compared to SUD (when the low exposure group was the reference). Only those exposed to violence compared to the low exposure group were more likely to have COD than psychiatric disorder: there was no difference between those exposed to sexual abuse and the low exposure group for COD and psychiatric disorder.

Table 4.6 Multinomial Logistic Regression of COD Outcomes with LCA Classes

	Model 4.2: Co-occurring Disorder Relative to								
	A: No Disorder			B: Psychiatric Disorder Only			C: Substance Use Disorder Only		
Characteristic	RRR		SE	RRR		SE	RRR		SE
Childhood Poverty (/no)	1.105		0.063	1.008		0.068	1.215	ǂ	0.079
Childhood Adversity (LCA) (/Class 3 "Low exposure")									
Class 1 ("Exposed to sexual abuse")	4.836	***	0.688	1.249	ǂ	0.145	3.616	***	0.639
Class 2 ("Exposed to violence")	2.592	***	0.160	1.188	**	0.082	2.238	***	0.148
Model Statistics: Design df = 113, F (54,60) = 147.56, p <0.001									

Note: Model is estimated with each comparison relative to COD as the reference group, RRR are re-parameterized to show COD relative to the comparison outcome, model controls for age, gender, race/ethnicity, nativity status, childhood family composition, family history variables, family support, childhood poverty, and age at first substance use.
SE = robust standard error, RRR = relative risk ratio, / = omitted reference category
ǂ p<.05; ** p<.01; *** p<.001, Analytic significance level is set to p=0.01 to account for multiple comparisons

4.2.8. Final Operationalization of Childhood Adversity

In determining how to operationalize childhood adversity for the remaining analyses, the results of the LCA and the other two childhood adversity measurement analyses were considered together. The criteria used for the decision were: distribution of the variables, and representativeness of both the number and frequency of adverse events.

The latent class examination highlighted the importance of isolating sexual abuse, especially, from the other childhood adversities because this group of people have such high relative risk ratios for COD. However, since the LCA yielded one group with only 3% of the sample in it and reduced all 24 adversities into just three classes (representing significant information loss), it is not ideal to keep the LCA categories as the main operationalization of childhood adversity. The LCA clearly pointed out the separate and dramatic effect of sexual abuse with COD, and the type of adversity analyses supported this as well. Therefore, a variable for sexual abuse frequency is warranted based on these findings.

The type of adversity analysis seen in Table 4.4 also highlighted the importance of verbal abuse for COD, which seemed to co-occur with physical abuse for Class 2 (those exposed to violence) in the LCA. The co-occurrence of physical and verbal abuse in the LCA and the importance of both physical and verbal abuse frequency for COD risk in the frequency analysis (Table 4.4) suggest the value of creating a combined variable for physical/verbal abuse frequency.

Finally, the count of the number of adverse events before the age of 18 was associated with COD and has the advantage of including all measures of adversity together in a single variable, with a good range and distribution in the population. In addition, it was the only measure that distinguished relative risk of COD from all other outcomes.

The two frequency indicators are captured in the count, however, only as part of the total number of events, along with all the other events. Because sexual abuse and physical/verbal abuse turned out to be so insidious in their relationship with COD, it is important to also capture their frequency. When considered simultaneously as a set of the three measures, the frequency variables will be displaying the effects of the frequency of these types of abuse above and beyond their contribution to total exposure (aside from the fact that it contributes to a global effect of adversity). Put another way, the total count variable captures the linear association of any and all types of adversity assessed in this study including sexual abuse and physical/verbal abuse, and the sexual abuse variable, then, captures any additional effect of the frequency of this type of adversity, as does the physical/verbal abuse frequency measure.

To summarize the final operationalization for the three variables used going forward in the analyses: the count variable for overall number of adversities (out of a possible 24) was created by summing the number of adverse events (Y/N) that ever occurred before age 18 (range 0-20, truncated to 15). Frequency of sexual abuse was calculated by taking the average of the frequencies reported for each of the four sexual abuse variables (reported on a scale of 0-4 where 0 represented “never” and 4 represented “very often”). Frequency of verbal/physical abuse was calculated by taking the average of the frequencies reported for each of the verbal (two questions) and physical abuse (three questions) variables (each reported on a scale of 0-4 where 0 represented “never” and 4 represented “very often”), for a total frequency score averaged across five variables.

4.3 Childhood Poverty and COD

4.3.1 Bivariate Associations of Childhood Poverty and Disorder

After concluding the examination of the childhood adversity operationalizations, and the preliminary analysis for the multinomial logistic regression, I began the analysis for Aim 1 of the dissertation, which tests whether there is an association between childhood poverty, childhood adversities, and lifetime COD. Specifically, this section describes their associations with lifetime occurrence of COD relative to no disorder, relative to psychiatric disorder only, and relative to SUD only. Because COD is a categorical outcome with four possible categories, the focal relationships in this Aim are interpreted in relation to all three comparisons. I present all three comparisons to highlight COD as a disorder that is different from psychiatric disorder only or SUD only. These comparisons allow conclusions to be drawn about the antecedents of lifetime COD in relation to the different possible disorder outcomes that comprise the COD measure.

Hypothesis 1a1 asserts that the experience of poverty in childhood will be associated with lifetime COD. Using bivariate multinomial logistic regression, experiencing childhood poverty, as measured by receiving government assistance before age 18, is significantly associated with COD with an RRR of 2.609 (model-based $t = 20.04$, $p<0.001$), or a 161% increase in likelihood, compared to no disorder: a large difference. When comparing bivariate relative risk associated with childhood poverty there is a 1.675 greater RRR ($t=9.32$, $p <0.001$) of COD compared to psychiatric disorder only, and a 1.798 greater RRR compared to SUD only ($t=9.79$, $p <0.001$) at the bivariate level. Thus, childhood poverty is associated with an added risk for COD, not just when compared to no disorder, but with both psychiatric and substance-related disorders as well (Adjusted Wald test, comparing the effect of poverty in childhood across all categories of COD, $F (3,111) = 143.62$, $p<0.001$).

4.3.2 Multivariate Model with Childhood Poverty and Disorder

The multivariate multinomial logistic regression in Model 4.3 (Table 4.7) shows the relationship of childhood poverty with all of the covariates found to be important in the preliminary analysis. The variables included in this model included: demographic variables (gender, race/ethnicity, nativity, age) family characteristics variables (family history, childhood family composition) and childhood experience variables (age of first substance use, family support, childhood poverty, and the three childhood adversity variables). This model tests whether or not the relationship between poverty and COD exists after accounting for all other variables (Hypothesis 1a1).

Model 4.3 comparisons A, B, and C are all obtained from the same multinomial logistic regression, and each model presents the risk ratios for COD relative to the other three disorder categories. With all covariates in the model, there is no overall direct association between poverty and disorder at the conservative $p<0.01$ level (as determined by a post-estimation Adjusted Wald test, comparing the effect of poverty in childhood across all 4 categories of COD, $F(3,111) = 3.56$, $p=0.017$). The conservative $p<0.01$ level is used to account for multiple comparisons. As Table 4.7 shows, this association is only significant between childhood poverty and COD relative to SUD (RRR of 1.203 of COD, $t=2.78$, $p = 0.006$) but not relative to psychiatric ($t= -0.27$, $p=0.791$) or no disorder ($t = 1.32$, $p=0.190$), and not overall. The model with all variables included and no conditional relationships can be seen in Table 4.7.

Hypothesis 1a2 posits that childhood adversities will be associated with lifetime occurrence of COD and will partially explain the association of childhood poverty and COD. The proper test of mediation was not possible in this study because of the mathematical uncertainty in estimating indirect effects in path analyses with multinomial outcomes. Although

the optimal test of this hypothesis was not possible, it is instructive to look at the relationship between childhood poverty and COD at the bivariate level and then again after the childhood adversity variables are included in the model. On a bivariate level, childhood poverty is directly associated with COD, and with the addition of the three childhood adversity variables there is still a direct association between poverty and COD (Adjusted Wald test $F(3,111) = 30.30$, $p<0.001$). When all other covariates are added, as with Model 4.3 in Table 4.7, childhood poverty is no longer significant in the model. This suggests, inferentially, that the relationship between poverty and COD outcomes is operating indirectly or is spurious, but does not suggest that the association between childhood poverty and COD is accounted for by childhood adversity. These models do not enable proper detection of whether the relationship is mediated through adversity.

Table 4.7 below shows the RRR and SE values for Model 4.3, a multinomial logistic regression of COD regressed on all covariates, childhood poverty, and childhood adversity variables.

Table 4.7 Multinomial Logistic Regression of COD Outcomes on All Covariates, Childhood Poverty, and Childhood Adversity

	Model 4.3: Co-occurring Disorder Relative to								
	A: No Disorder			B: Psychiatric Disorder Only			C: Substance Use Disorder Only		
Characteristic	RRR		SE	RRR		SE	RRR		SE
Age (years)	0.980	***	0.002	0.980	***	0.002	0.998		0.002
Male (/female)	1.058		0.051	1.925	***	0.107	0.518	***	0.031
Race (/NH White)									
NH Black	0.565	***	0.045	0.759	***	0.053	0.857		0.065
NH Asian American	0.553	***	0.072	0.648	**	0.081	0.640	**	0.089
Hispanic	0.664	***	0.043	0.885		0.068	0.987		0.074
US-Born (/foreign born)	2.287	***	0.199	1.717	***	0.163	1.075		0.116
Childhood family structure (/two biological parents)									
Reconstituted families	0.902		0.059	0.937		0.060	0.846	ǂ	0.059
Single parent	0.914		0.054	0.924		0.067	0.875		0.066
Other	1.130		0.152	0.919		0.137	1.212		0.196
Family support (/no)	1.209	ǂ	0.067	1.126		0.067	1.090		0.076
Family history variables									
Family history COD (/no COD)	2.756	***	0.165	1.404	***	0.080	1.785	***	0.115
Family history unknown (/known)	1.504	***	0.164	0.937		0.116	1.443	**	0.170
Family history SUD (/no SUD)	1.680	***	0.119	1.419	***	0.099	1.058		0.078
Family history psychiatric disorder (/no psych disorder)	2.603	***	0.152	1.006		0.049	2.406	***	0.117
Age at first substance use	0.821	***	0.007	0.826	***	0.008	0.962	***	0.008
Childhood Poverty (/no)	1.078		0.061	0.970		0.065	1.203	***	0.077
Childhood Adversity Variables									
Childhood Adversities (Count)	1.089	***	0.011	1.042	***	0.010	1.048	**	0.015
Early Sexual Abuse (Freq)	1.556	***	0.108	0.984		0.048	1.521	***	0.120
Early Verbal and Physical Abuse (Freq)	1.433	***	0.070	1.041	ǂ	0.046	1.292	***	0.076

Model Statistics: Design df = 113, F (57,57) = 147.25, p <0.001

Note: Model is estimated with each comparison relative to COD as the reference group, RRR are re-parameterized to show COD relative to the comparison outcome

SE = robust standard error, RRR = relative risk ratio, / = omitted reference category

ǂ p<.05; ** p<.01; *** p<.001, Analytic significance level is set to p=0.01 to account for multiple comparisons

4.4 Childhood Adversity and Disorder

4.4.1 Bivariate Associations of Childhood Adversity and Disorder

The operationalization of childhood adversities in this dissertation was discussed earlier in the chapter, now I interpret the results of the chosen operationalization of these three variables when they are used together in multinomial logistic regressions with lifetime COD: first on a bivariate level, and then in multivariate models. I do this because adversity is a key variable and the bivariate and multivariate examinations are instructive in understanding their association with COD.

Using bivariate multinomial logistic regression, number of childhood adversities is significantly associated with COD with an RRR of 1.269 (model-based t =44.63, p<0.001), or a 26.9% increase in likelihood, compared to no disorder. When comparing relative risk of COD to those who have only psychiatric disorder, each occurrence of childhood adversity has a 1.079 greater RRR (t=15.68, p <0.001) and a 1.074 greater RRR compared to SUD only (t=13.67, p <0.001) at the bivariate level. Childhood sexual abuse frequency is significantly associated with COD compared to no disorder, compared to psychiatric disorder only, and compared to SUD only (RRR=3.302, t=18.12, p <0.001, RRR= 1.141, t=4.04, p <0.001, and RRR=2.741, t=11.90, p <0.001, respectively). Childhood physical/verbal abuse frequency is also significantly associated with COD compared to no disorder, compared to psychiatric disorder only, and compared to SUD only (RRR=2.743, t=35.67, p <0.001, RRR= 1.311, t=12.32, p <0.001, and RRR=1.839, t=25.40, p <0.001, respectively) at the bivariate level.

4.4.2 Multivariate Model with Childhood Adversity and Disorder

In the multivariate multinomial logistic regression in Model 4.3 (Table 4.7 above) with all covariates included, all three childhood adversity variables are significantly associated with

disorder outcomes as determined using post-estimation Adjusted Wald tests: for the adversity count variable ($F(3,111) = 22.37$, $p<0.001$); for sexual abuse frequency ($F(3,111)=27.46$, $p<0.001$); and for physical/verbal abuse frequency ($F(3,111)=24.48$, $p<0.001$).

The magnitude of the association for each of these adversity measures with COD depends on the outcome being compared, as shown in Table 4.7. For example, comparing COD to no disorder, the childhood adversity count has an RRR of 1.089. Sexual abuse frequency has an RRR of 1.556 for COD relative to no disorder and physical and verbal abuse frequency has an RRR of 1.438 for COD relative to no disorder (associated test statistics seen in Model 4.3, Table 4.7). However, when comparing COD to psychiatric disorder, each occurrence of childhood adversity (in the count measure) only adds a 1.042 RRR ($t=4.69$, $p<0.001$). For this comparison, the frequency measures are non-significant. For COD relative to SUD, the adversity variables are all significant: the count of adversities and the frequency of abuse variables are all associated with a larger relative risk of COD.

Across all three comparisons, the effect of the number of adverse experiences on COD is relatively small and relatively stable across disorder outcomes, adding between a 4.2 and 8.9% increase in COD risk relative to any other disorder outcomes, net of other covariates in the model and frequency measures. Both abuse frequency variables are associated with larger relative risk ratios for COD vs. no disorder and for COD vs. SUD, with sexual abuse frequency adding about 1.5 times the risk for COD in both comparisons and each increase in verbal/physical abuse frequency adding about 1.3-1.5 times the risk for COD vs. no disorder and for COD vs SUD.

4.4.3 Covariates in the Multivariate Model with Childhood Poverty, Adversity and Disorder

Concerning the other covariates in Model 4.3: demographic variables are especially important in differentiating COD from the three outcomes being compared. Age is negatively

associated with COD compared to no disorder and psychiatric disorder only (where people with COD are younger, on average, than the other two groups), but not SUD only. Being male relative to female is associated with COD, especially relative to psychiatric disorders only: where males are twice as likely to have COD than a psychiatric disorder only. Conversely, males are about half as likely to have COD as they are to have SUD. There are no gender differences between those with COD and those with no disorder. There are significant differences in terms of disorder outcomes by race/ethnicity (as determined using a post-estimation Adjusted Wald test ($F(9,105) = 51.03$, $p<0.001$)). Blacks are less likely than Whites to have COD when compared to the no disorder and psychiatric disorder only. Asian Americans are less likely than Whites to have COD across all comparisons. Hispanics and Whites differ in their likelihood of COD relative to no disorder, but not COD relative to other outcomes. Being born in the US (relative to being born in another country) is associated with a large relative risk of COD compared to no disorder, as well as COD compared to psychiatric disorder only.

The variables representing family characteristics in Model 4.3 are mixed in terms of their overall contributions to understanding COD risk. Childhood family structure and family support are not significant, net of other explanations, in their association with COD (as determined using two post-estimation Adjusted Wald tests ($F(9,105) = 1.55$, $p = 0.141$ and $F(3,111) = 1.05$, $p = 0.373$, respectively). However, the family history variables are significantly associated with COD – possibility indicating genetic transmission of risk and possibly indicating some shared environments that elevate COD likelihood. In the case of biological maternal or paternal history of COD, this increases the relative risk of COD compared to all other disorder outcomes. Having family history of psychiatric disorder is associated with COD as well, but only compared to those with no disorder and those with SUD only, not compared to those with psychiatric disorder.

Family history of SUD only is associated with COD relative to no disorder and psychiatric disorder, but not relative to SUD only. Not knowing your family history is associated with COD relative to SUD only and no disorder.

The bulk of the childhood experience variables in this model have already been discussed above (childhood poverty and the three childhood adversity variables). These childhood experiences matter to COD, above and beyond the other explanations for development of a disorder. Age of first substance use is negatively associated with COD, relative to all other outcomes.

4.5 Chapter Summary

This chapter showed a high prevalence of childhood adversity in all racial/ethnic and gender groups in the population, with variation within these social status categories. Particular childhood adversities clustered in three groups in the population, and these three latent classes were used to create the final operationalization of childhood adversity for the dissertation, along with the two other measures tested. Using the optimal measures of adversity, childhood poverty, and all other covariates, a multinomial logistic regression was estimated to examine the focal relationship between childhood poverty and disorder outcomes. The association between childhood poverty and COD was significant at the bivariate level but not at the multivariate level, when controlling for adversity and other alternative associations. In contrast, all three childhood adversity variables are significantly associated with disorder outcomes both at the bivariate and multivariate level.

CHAPTER 5:

RACIAL/ETHNIC AND GENDER DIFFERENCES IN CHILDHOOD POVERTY, CHILDHOOD ADVERSITY, AND CO-OCCURRING DISORDER

In this Chapter, I examine conditional relationships between childhood poverty and disorder as well as childhood adversity and disorder, by race/ethnicity and by gender, according to the analysis plan described Chapter 3. In doing so, this chapter seeks to uncover the untested assumptions that are pervasive in COD research, namely, that the relationships between early life social conditions and later development of COD are operating in the same way for males and females as well as for different racial/ethnic groups. The conditional relationships tested in this chapter begin with the introduction of product interaction terms that examine variation by gender, and then move on to the use of product interaction terms that examine variation by race/ethnicity. These analyses begin with the whole sample, and when conditional relationships are found, the analysis is stratified by gender to aid in interpretation. The stratified analyses demonstrate that childhood poverty and childhood adversity are both significant factors in differentiating relative risk of disorder outcomes for males and females.

5.1 Conditional Relationships by Gender

In accordance with the theoretical underpinnings of this dissertation, I examine the centrality of gender as a factor that determines membership in status groups and correspondingly impacts exposure to stressors. I look for variations in the focal relationship by gender, to see if the association between childhood poverty and COD operates differently for males and females, and I also test whether the impact of childhood stressors on COD operates differently for these groups.

5.1.1 Childhood Poverty and Count of Adversities Conditional on Gender for COD

Model 4.3 (Table 4.7), with all covariates and childhood poverty and adversity variables, described in Chapter 4 assumes by default that the relationships between childhood poverty and disorder as well as childhood adversity and disorder are operating the same for males and females. These assumptions are countered with two alternative hypotheses: 1) Hypothesis 1c1, which states that childhood adversities will affect COD differently by gender, and 2) Hypothesis 1c2, which posits that childhood poverty will be more strongly associated with COD in males than females. Interaction terms testing the relationship between the count of childhood adversities and gender, and the relationship between childhood poverty and gender are introduced first into separate models, each with the full set of covariates, childhood poverty, and childhood adversity variables, creating Models 5.1a and 5.2.

In Model 5.1a, which has the interaction term childhood adversity count × gender, this conditional relationship was present, as indicated by a statistically significant p value for the product interaction term (determined with a post-estimation Adjusted Wald Test $F(3,111) = 6.60$, $p<0.001$). In Model 5.2 testing the conditional relationship between childhood poverty and gender with the product interaction term childhood poverty × gender, a statistically significant p value for the interaction is also present ($F(3,111) = 6.79$, $p<0.001$). Models not shown.

This presents an interesting situation: both poverty and adversity are found to be conditional on gender in separate models, and if this is truly the case, then these two relationships should be interpreted only while taking into account each other, to avoid drawing incorrect conclusions about the nature of poverty, adversity, and COD. When I proceed to test the next logical step, by introducing a third order term for childhood poverty × childhood adversity count × gender, and its associated lower-order terms, into a model that contains the full

set of covariates, childhood poverty, and childhood adversity variables, I find that this three-way interaction is not significant (Adjusted Wald Test, F (3,111) = 0.91, p=0.441, not shown). This three way interaction is tested in Model 5.8a. Models numbers are not sequential because of the order in which the hypotheses were tested.

To reconcile the findings between adversity and gender and poverty and gender, I then construct a model that accounts for both of these conditional relationships: Model 5.3 shown below in Table 5.1. This model includes both sets of significant interactions (i.e. childhood poverty × gender and childhood adversity count × gender) along with the other covariates from Model 4.3. When both sets of interactions are added to the same model, both remain significant (determined by using two post-estimation Adjusted Wald Tests with values of F (3,111) =5.62 p=0.001 for childhood poverty × gender; F (3,111) =5.23, p=0.002 for childhood adversity × gender). The model showing these two conditional relationships together is given in Table 5.1.

Table 5.1 below presents the relative risk ratios for COD relative to no disorder, psychiatric disorder only, and SUD only. Variables involved in the interactions as well as the type of childhood adversity variables are presented in the table, covariates are controlled for but not shown in the table.

Table 5.1. Multinomial Logistic Regression of COD Outcomes with Childhood Poverty Conditional on Gender and Childhood Adversity Conditional on Gender Model

	Model 5.3: Co-occurring Disorder Risk Relative to:								
	A: No Disorder			B: Psychiatric Disorder only			C: Substance Use Disorder only		
Characteristic	RRR		SE	RRR		SE	RRR		SE
Male (/female)	0.924		0.060	1.942	***	0.130	0.442	***	0.035
Childhood Poverty × Male	1.213		0.141	1.120		0.111	1.610	***	0.193
Childhood Poverty (/no)	0.977		0.077	0.919		0.076	0.899		0.083
Childhood Adversity Count × Male	1.030	**	0.014	0.986		0.010	1.014		0.015
Childhood Adversity Count	1.072	***	0.013	1.050	***	0.011	1.051	**	0.018
Other Childhood Adversity Variables									
Early Sexual Abuse (Freq)	1.613	***	0.118	0.981		0.050	1.554	***	0.122
Early Physical Abuse (Freq)	1.444	***	0.072	1.036		0.045	1.283	***	0.074

Model Statistics: Design df = 113, F (63,51) = 119.13, p <0.001

Note: Model is estimated with each comparison relative to COD as the reference group, RRR are re-parameterized to show COD relative to the comparison outcome, model controls for age, gender, race/ethnicity, nativity status, childhood family composition, family history variables, family support, childhood poverty, and age at first substance use.

SE = robust standard error, RRR = relative risk ratio, / = omitted reference category

ǂ p<.05; ** p<.01; *** p<.001, Analytic significance level is set to p=0.01 to account for multiple comparisons

5.1.2 Type of Adversity Conditional on Gender for COD

The interaction term for count of childhood adversities × gender tested first in Model 5.1a and then in Model 5.3 in Table 5.1 (in Model 5.3 it is tested along with childhood poverty × gender) makes it clear that the way adversities are associated with the development of disorders is not the same for males and females. However, it does not give an indication as to whether the associations between other measures of adversity and COD differ for males and females. To probe this further, and to test whether the frequency of sexual abuse and physical/verbal abuse also matter differently for males and females, two models are estimated each with an interaction

term between gender and the frequency of adversity variable. These models again each use the full set of covariates, childhood poverty, and childhood adversity variables, and they are depicted in the equations for Models 5.1b and 5.1c in Table 3.3. Models 5.1b is estimated to provide a test of alternative Hypothesis 1c1: that sexual abuse frequency will matter more for females than males. The conditional relationships between frequency of sexual abuse events and gender is not statistically significant (as indicated by an Adjusted Wald Test for the interaction term frequency of sexual abuse × gender F (3,111) = 1.27, p=0.287) in Model 5.1b. Using Model 5.1c, I test whether frequency of physical/verbal abuse events affect COD differently by gender, and based on the non-significant interaction term frequency of physical/verbal abuse × gender in this model (Adjusted Wald Tests for the interaction term F (3,111) = 3.34, p=0.022), I find no evidence of such a conditional relationship.

Finding no additional conditional relationships by gender, Model 5.3 in Table 5.1 (with the two gender interaction terms) is left as the model that most accurately shows the way that poverty and adversity operate differently based on whether a person is male or female. Model 5.3 in Table 5.1 shows that both childhood poverty and the count of childhood adversities are associated with COD, controlling for alternative explanations, however their relationship with disorder outcomes depends on gender.

Model 5.3 in Table 5.1 shows how poverty and adversity are conditional on gender for COD, and I interpret these interactions from the conditional model here. For A: COD relative to no disorder, the significant RRR of 1.030 (SE 0.014, p =0.007) for the childhood adversity count × gender interaction indicates the effect that childhood adversity for males has relative to the effect that childhood adversity has for females, and shows that the number of adversities has a larger effect for males, in risk of COD, net of other factors. The childhood adversity count

variable in this comparison has an RRR of 1.072 (SE = 0.013, p<0.001), showing that for females, controlling for the effect of all other covariates, each additional adversity is associated with a 7.2% increase in relative risk of COD compared to no disorder. For males, the effect of childhood adversity is the product of the coefficient for count of adversity and the interaction term, thus, each adversity is associated with a 10.4% increase in the relative risk of COD vs. no disorder for males (RRR = 1.104, SE = 0.015, p<0.001). The lack of a statistically significant RRR for the gender coefficient in the model indicates that, in the absence of poverty and with zero adversities in childhood, there is no difference in the RRR of males relative to females for the development of COD relative to no disorder. The non-significant RRR for the childhood poverty variable indicates that it does not have a statistical association with COD risk, relative to no exposure to poverty for males (RRR = 1.185, SE = 0.099, p =0.046) or for females (RRR = 0.977, SE = 0.077, p = 0.770). Above and beyond the conditional effects of the count of adversities, the frequency of early sexual abuse and the frequency of early physical/verbal abuse are both significantly associated with greater risk for COD relative to no disorder.

Now I draw attention to the comparison B: between COD and psychiatric disorder only. The significant co-efficient for male in this comparison indicates that males are significantly more likely (nearly two times more likely) to have COD than psychiatric disorder only, relative to their female counterparts in the absence of poverty and adversity. The coefficient for count of childhood adversities is also significant in this model, such that for males each adversity experienced increases the RRR of COD vs. psychiatric disorder only by 1.050 (SE = 0.011, p<0.001). The absence of a statistically significant interaction term for count of childhood adversities × gender indicates that the effect of the total number of adversities on COD vs. psychiatric disorder likelihood does not differ for males and females. The lack of significance of

the childhood poverty × gender interaction means that the effect that childhood poverty has on COD does not differ for males and females for this comparison. Neither the frequency of early sexual abuse nor the frequency of early physical/verbal abuse are associated with COD relative to no disorder, net of all other covariates in this model.

Finally, I discuss the conditional relationships that gender has in the comparison of C: COD to SUD only. The significant RRR of 1.610 (SE 0.193, p <0.001) for the childhood poverty × gender interaction indicates the effect that childhood poverty has for males relative to the effect that childhood poverty has for females, and shows that poverty has a larger effect on increasing COD vs. SUD relative risk for males than females, net of other factors. The childhood adversity count variable in this comparison has an RRR of 1.051 (SE = 0.018, p<0.001), showing that for females, controlling for the effect of all other covariates, each additional adversity is associated with a 5.1% increase in relative risk of COD compared to SUD only. The co-efficient for childhood poverty is not significantly associated with COD here, meaning that for females, poverty does not differentiate COD risk from SUD only risk. However, childhood poverty has an RRR of 1.448 (SE = 0.123, p<0.001) for males and is significantly associated with more risk of COD, showing that for males with childhood poverty, there is an added 44.8% risk of COD relative to SUD only. The coefficient for gender in this model shows that males are much less likely than females to have COD compared to SUD only (RRR=0.442, SE=0.035, P<0.001) in the absence of poverty and adversity. Under these circumstances, females, then are more than twice as likely to have COD than SUD only (RRR for females = 2.262, SE= 0.181, p<0.001).

5.1.3 Predicted Probability of COD, SUD, Psychiatric Disorder, and No Disorder Given Conditional Gender Relationships

The predicted probabilities are generated using the margins command with other covariates at their means and based on Model 5.3, Table 5.1. The graphs are a helpful depiction of the conditional gender and childhood adversity and gender and childhood poverty differences described in the previous section, keeping in mind that in the previous section COD risk was interpreted relative to one other outcome in each comparison. The predicted probabilities look at the likelihood of each disorder status relative to all of the other disorder outcomes for the males and females being compared.

Figure 5.2a shows the predicted probability of having no disorder across the count of childhood adversities, for males and females with and without poverty. Based on the dydx command, which assesses the statistical significance of the marginal effect of variables based on the predicted probabilities for each outcome at different values/categories of adversity, poverty, and gender, it is possible to interpret the trends seen in Figures 5.2a-d. For the probability of no disorder, this likelihood decreases for males as well as females as the numbers of childhood adversities increase (dy/dx= -0.021, SE = 0.003, $p<0.001$ for males, and dy/dx= -0.015, SE = 0.002, $p<0.001$ for females). There is no statistically significant difference in the predicted probability for either males with and without poverty or females with and without poverty (dy/dx= -0.007, SE = 0.017, p=0.664 for males and dy/dx= -0.011, SE = 0.016, p=0.487 for females).

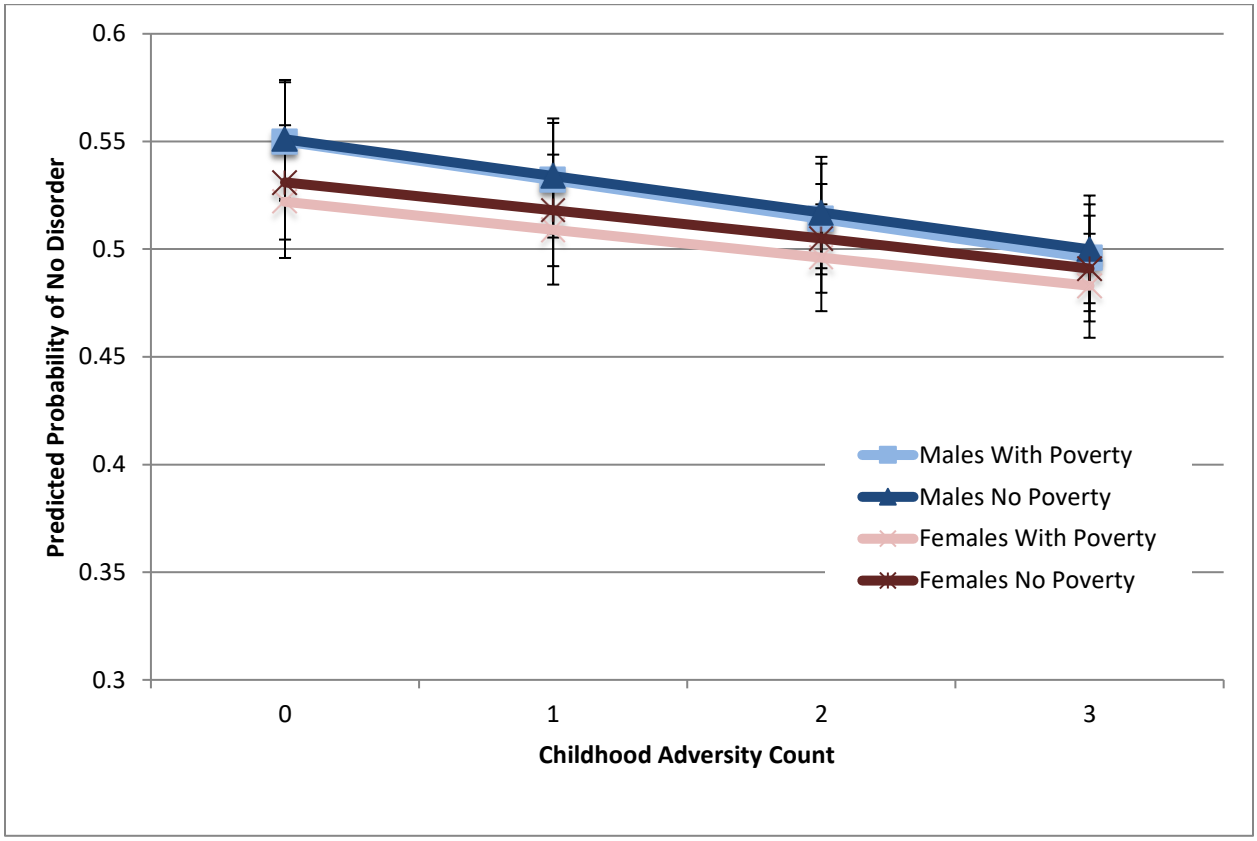
To see the predicted probability of COD as an outcome, refer to Figure 5.2b. For males, more adversities in childhood are associated with a higher probability of COD (dy/dx= 0.008, SE = 0.001, $p<0.001$). Males with childhood poverty are more likely than all other groups to have

COD (including males without childhood poverty, dy/dx= 0.013, SE = 0.006, p=0.026 for that comparison). For females with childhood poverty, the direction of the association is reversed: COD is less likely as an outcome than it is for females without childhood poverty, however, the predicted probabilities are not statistically different from each other (dy/dx= -0.003, SE = 0.005, p=0.434). For females, number of adversities are associated with increased predicted probability of COD as an outcome (dy/dx= 0.006 SE = 0.001, p<0.001).

For the outcome of psychiatric disorder only, poverty does not make a statistically significant difference for either gender in predicted probability of disorder, as seen in Figure 5.2c and as indicated by non-significant dy/dx comparisons (dy/dx= 0.023, SE = 0.012, p=0.067 for males, dy/dx= 0.011, SE = 0.014, p=0.449 for females). Overall, females are much more likely to have psychiatric disorder only than males, and the predicted probability of psychiatric disorder for both males (dy/dx= 0.010, SE = 0.001, p<0.001) and females (dy/dx= 0.008, SE = 0.002, p<0.001) increases as the number of adversities increases.

For SUD only, number of adversities does not make a difference for either gender (dy/dx= 0.002, SE = 0.001, p=0.225 for males, dy/dx= 0.001, SE = 0.001, p=0.577 for females), but poverty does. Males with no poverty have the highest predicted probability of this event, overall, and males with childhood poverty have the next highest predicted probability of SUD (dy/dx= -0.029, SE = 0.009, p=0.004 for males with and without poverty). Childhood poverty is not significantly associated with SUD only for females, thus, females with or without poverty do not have a statistically different predicted probability of SUD, all other factors held constant (dy/dx= 0.004, SE = 0.005, p=0.425). See Figure 5.2d for the predicted probability of SUD only for females and males with and without childhood poverty across different numbers of childhood adversities.

Figure 5.2a. Predicted Probability of No Disorder Outcome by Gender, Childhood Poverty, and Number of Adversities



All predicted probabilities are on plotted the same scale (0.0-0.3), except the predicted probability of no disorder, which is instead depicted on a scale of 0.3-0.6 to be displayed optimally.

Figure 5.2b. Predicted Probability of Co-occurring Disorder Outcome by Gender, Childhood Poverty, and Number of Adversities

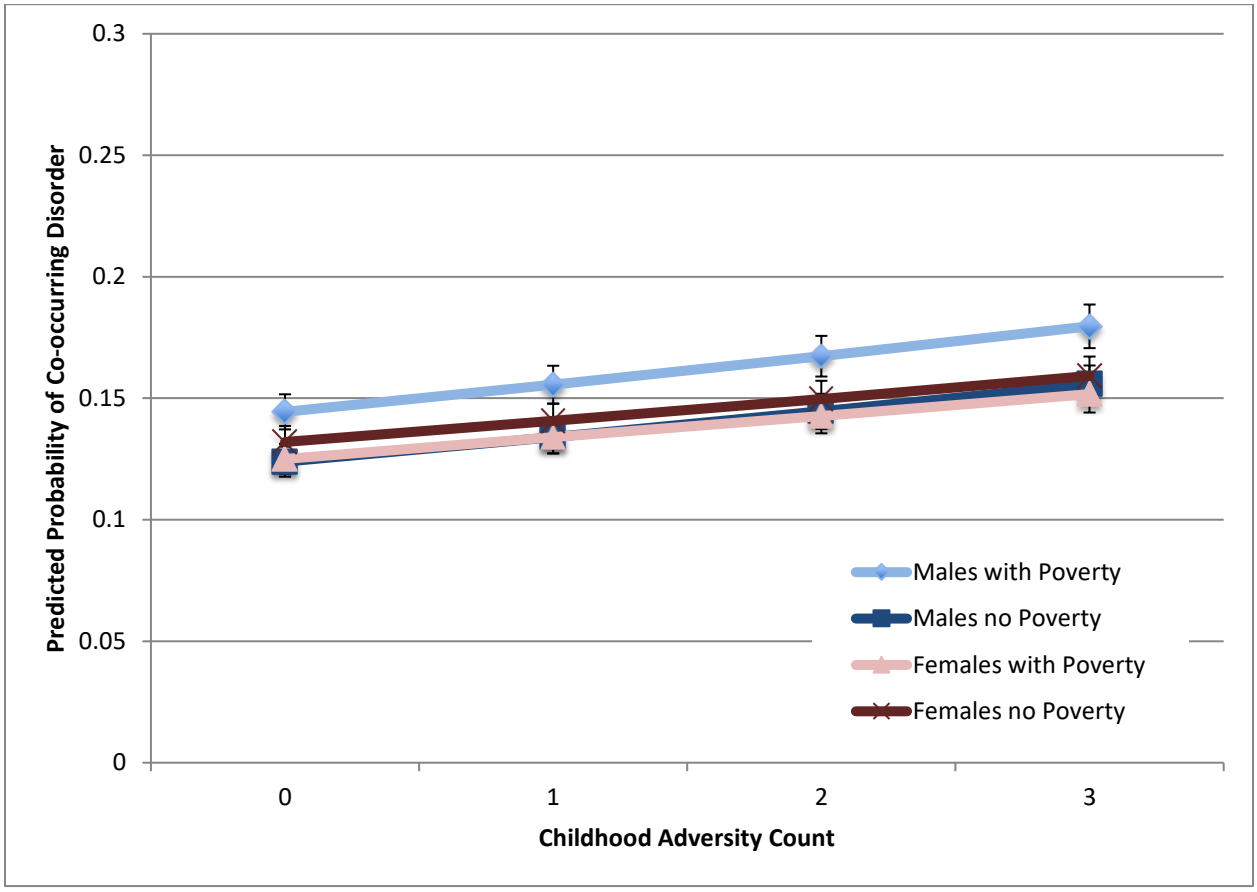


Figure 5.2c. Predicted Probability of Psychiatric Disorder Only Outcome by Gender, Childhood Poverty, and Number of Adversities

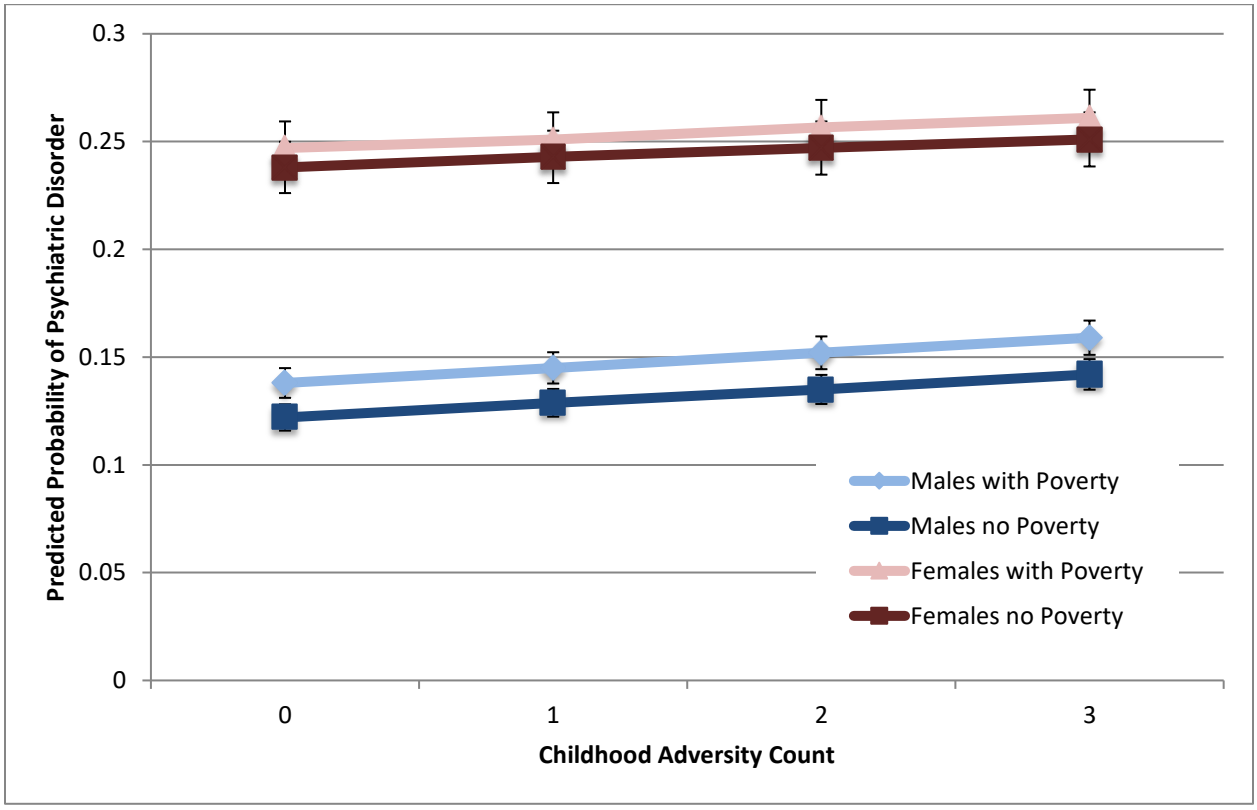
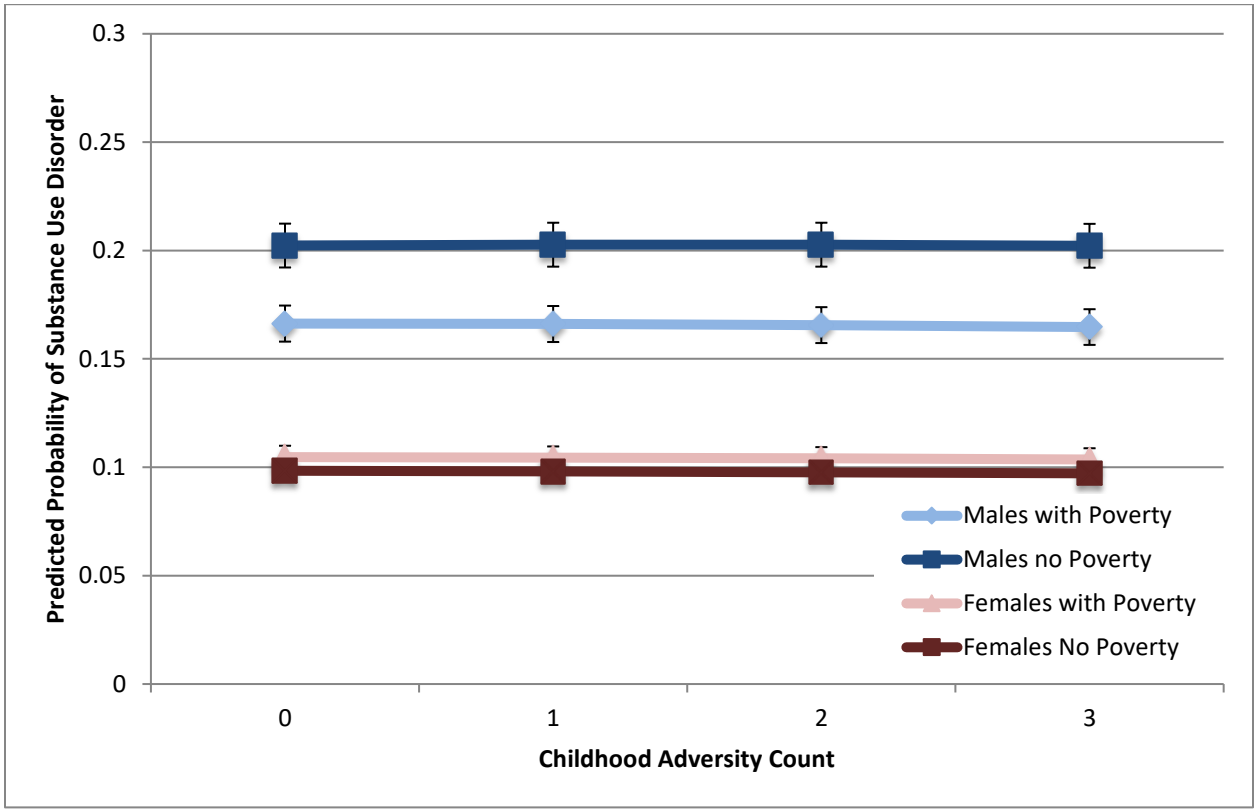


Figure 5.2d. Predicted Probability of Substance Use Disorder Only Outcome by Gender, Childhood Poverty, and Number of Adversities



Since both of these relationships (childhood poverty and COD and childhood adversity and COD) are conditional on whether someone is male or female, for clarity of interpretation, I stratify the analysis by gender to show the relationships separately for males and females. The focal relationships are thus presented for males and females in the corresponding sections of this chapter.

5.2 Childhood Poverty, Adversity, and Disorder for Males

Due to the gendered nature of psychiatric disorders, it is possible that processes of disorder development occur in different ways for males and females: a possibility I allow for but do not test when stratifying the analyses by gender. For males, both COD and SUD are more

common outcomes than just psychiatric disorder alone. Based on Hypothesis 1c2, I expect that childhood poverty will be more strongly related to COD when the comparison group is psychiatric disorder than when the comparison is SUD only for males. To test this, and to show the focal relationship between poverty and COD for males, net of other explanations and controls, Model 5.4 in Table 5.2 estimates a multinomial logistic regression for disorder outcomes restricted to males.

Table 5.2 below presents the relative risk ratios just for males for COD relative to no disorder, psychiatric disorder only, and SUD only as well as the robust standard errors and significance levels for each estimate.

Table 5.2 Multinomial Logistic Regression of COD Outcomes, Males Only (n=14,763)

	Model 5.4: Co-occurring Disorder Risk Relative to:								
	A: No Disorder			B: Psychiatric Disorder Only			C: Substance Use Disorder Only		
Characteristic	RRR		S.E.	RRR		SE	RRR		SE
Age (years)	0.980	***	0.002	0.980	***	0.003	0.997		0.003
Race (/NH White)									
NH Black	0.661	***	0.066	0.807	ǂ	0.087	0.988		0.093
NH Asian	0.493	***	0.094	0.446	***	0.092	0.607	ǂ	0.121
Hispanic	0.666	***	0.067	0.802		0.094	0.999		0.096
US-Born (/foreign born)	2.079	***	0.254	1.379	ǂ	0.187	0.965		0.130
Childhood family structure (/two biological parents)									
Reconstituted families	0.879		0.080	0.951		0.100	0.929		0.075
Single parent	0.927		0.081	0.938		0.108	0.946		0.090
Other	1.154		0.246	0.885		0.191	1.395		0.332
Family support (/no)	1.160		0.099	1.101		0.106	1.143		0.108
Family history variables									
Family history COD (/no COD)	2.516	***	0.243	1.196		0.117	1.703	***	0.155
Family history unknown (/known)	1.572	**	0.199	0.995		0.187	1.548	**	0.224
Family history SUD (/no SUD)	1.915	***	0.168	1.419	**	0.161	1.114		0.106
Family history psychiatric disorder (/no psych disorder)	3.022	***	0.208	1.074		0.089	2.475	***	0.151
Age at first substance use	0.811	***	0.009	0.814	***	0.009	0.956	***	0.009
Childhood Poverty (/no)	1.177		0.106	1.042		0.092	1.411	***	0.124
Childhood Adversity Variables									
Childhood Adversities (Count)	1.104	***	0.019	1.058	***	0.017	1.071	**	0.020
Early Sexual Abuse (Freq)	1.540	**	0.221	0.918		0.091	1.708	**	0.263
Early Physical Abuse (Freq)	1.459	***	0.103	0.950		0.064	1.251		0.098

Model Statistics: Design df = 113, F (54, 60) = 48.66, p <0.001

Note: Model is estimated with each comparison relative to COD as the reference group, RRR are re-parameterized to show COD relative to the comparison
SE = robust standard error, RRR = relative risk ratio, / = omitted reference category
ǂ p<.05; ** p<.01; *** p<.001, Analytic significance level is set to p=0.01 to account for multiple comparisons

5.2.1 COD Relative to No Disorder for Males

I now review the findings for each disorder comparison, beginning with COD relative to no disorder. It is interesting to look at how the key variables in the study differ relative to these two outcomes being compared, as this shows the most extreme comparison of outcomes: predicted probability of COD relative to having no disorder. This comparison illustrates the factors that drive poor outcomes for COD when the comparison is psychologically healthy males.

Childhood experiences are substantial contributors to relative risk of COD. As shown in Table 5.2, for COD relative to no disorder, the experience of childhood poverty does not significantly change the likelihood of COD. Increases in number of adversities do, though. These are associated with increased probability of COD: with each adversity experienced, the relative risk of COD increases by 10.4% (RRR 1.104, t= 5.78, p<0.001), net of other variables in the model. Sexual abuse frequency and physical/verbal abuse frequency are both associated with large increases in the relative risk of COD for males, over and above the count of adversities, and these represent critical experiences before the age of 18 that, when they occur with increasing frequency, separate likelihood of COD from likelihood of no disorders in one's lifetime. For the last childhood experience variable, age of first substance use, the younger males are when they use alcohol or drugs for the first time, the higher their risk of COD relative to no disorder.

Demographics help to distinguish relative risk of COD from no disorder. Blacks and Hispanic males are only two-thirds as likely as White males to have COD when compared to no disorder and Asian Americans are 49.3% as likely as Whites to have COD (RRR= 0.493, t=-3.72, p<0.001). Age is negatively associated with COD risk for males, meaning that younger age

is more highly associated with COD. Being born in the US comes with a higher RRR for COD than being born elsewhere.

For familial characteristics, some variables matter more than others in this model. Family history is a variable that has large and significant relative associations with COD. Each type of family history is associated with higher relative risk of COD than no disorder. Psychiatric disorder in a biological parent has the largest association, increasing relative risk by over 200% (RRR =3.022, t= 16.09, $p<0.001$) relative to no parental disorder, but COD in a parent, SUD in a parent, and even not knowing your family history (relative to no parental disorder) are all still strongly associated with large increases in relative risk of COD compared to no disorder. As seen in Table 5.2, the other familial characteristics do not have statistically significant associations: childhood family structure and childhood family support are not independently associated with COD.

5.2.2 COD Relative to Psychiatric Disorder for Males

Comparing the relative risk of developing psychiatric disorder in conjunction with SUD (i.e. COD) to just the development of psychiatric disorder is telling. The comparisons in this section show the factors that distinguish the often more severe outcome of COD from the development of a psychiatric disorder without SUD.

Poverty does not make a significant difference for males in differentiating COD from psychiatric disorder, and neither does frequency of sexual or physical/verbal abuse. The count of childhood adversities is significant, though: for each additional stressor in childhood, the relative risk for the outcome of COD compared to psychiatric disorder increases by 5.8% (RRR = 1.058, t=3.61, $p<0.001$). These associations, and the others presented in this section, can be seen in Table 5.2 (comparison 'B'). Again, as with the comparison between COD and no disorder, age

of first substance use is significantly associated with the development of COD, Thus, it seems that number of adversities and age that males first get introduced to alcohol or drugs are critical childhood factors in likelihood of acquiring COD over psychiatric disorder by itself.

Only a few demographic factors distinguish these two outcomes from each other. Age is negatively associated with COD risk for males (RRR = 0.980, t=-7.60, p<0.001) and Asian American males are only 44.6% as likely as White males to have COD (RRR= 0.446, t=-3.90, p<0.001) than psychiatric disorder, but the other demographics do not make a difference.

Again, family history variables are the only familial characteristics that are significantly associated with COD compared to psychiatric disorder, and here it is just family history of SUD (compared to no parental disorder) that increases the relative risk of COD.

5.2.3 COD Relative to SUD for Males

The comparisons in this section show the factors that distinguish COD from the more common male disorder outcome of SUD only and are instructive in highlighting the different characteristics that may set males apart in the development of these two types of disorders.

In this comparison, as seen in Model 5.4 in Table 5.2 (comparison 'C'), the childhood experience variables are mostly significant in the relative risk ratios for COD, and many of the other demographic and familial variables are not. For the difference between acquiring COD and SUD, childhood poverty matters: males who grow up in households receiving government assistance are more likely to have SUD in conjunction with psychiatric disorder (i.e., COD) as an outcome than SUD only (RRR=1.411, t=3.91, p<0.001), net of other factors. Frequency of sexual abuse differentiates COD from SUD as well, but frequency of physical/verbal abuse does not. The count of adversities is also associated with COD. Similar to the results seen in the

previous two sections of comparisons for males, age of first substance use is negatively associated with COD vs. SUD alone.

Psychiatric disorder in a biological parent is associated with a large and significant RRR for COD vs. SUD (Model-based RRR =2.475, t=14.81, p<0.001). COD in a parent and family history being unknown are also important factors associated with COD risk, but they are associated with smaller relative risk ratios than familial psychiatric disorder.

In contrast to the other comparisons in this model (comparisons 'A' and 'B' in Model 5.4), none of the demographic factors are associated with COD risk relative to SUD.

5.2.4 Trends in Factors Associated with Relative Risk Ratios of COD for Males

After presenting the results for males by each disorder comparison, I offer some analysis of the overall trends in the results just presented, here. In doing so, I am switching from looking at trends in columns A, B, and C in Table 5.2 to instead describing differences across the rows of particular variables, highlighting the ones that show interesting results and highlighting similarities and differences across the outcomes.

Childhood experiences in general separate relative risk ratios of COD from other disorder outcomes for males, although different variables are significant in different comparisons. The only place childhood poverty is statistically significant is where it increases the RRR of COD relative to SUD. The count of adversities, in contrast, is associated with a higher relative risk of COD no matter what the outcome of comparison. Frequency of sexual abuse increases RRRs for COD vs. SUD and COD vs. no disorder. Frequency of physical/verbal abuse only differentiates COD from no disorder.

Childhood family structure and childhood family support are not independently associated with COD, in any of the models, whereas age of first substance use is associated with

COD relative to all outcomes: the younger males are when they first use substances, the higher their risk of COD.

Family history of a variety of types of disorders provide large and significant associations with COD for all of the comparisons made in this section, although the types of disorders vary in terms of their significance with COD across different comparisons.

Lastly, race/ethnicity is most significant in the comparison between COD and no disorder, where all other racial/ethnic groups have lower RRR of COD than Whites. The only other significant racial/ethnic difference is for COD relative to psychiatric disorder, where Asian American males have lower relative risk of COD than White males.

5.3 Childhood Poverty, Adversity, and Disorder for Females

In accordance with the theory that psychiatric and SUD develop in unique ways for males and females: I now look at the results of the stratified analysis for females only. For females, the most prevalent outcome is psychiatric disorder alone, a phenomenon detailed in the *Sample Characteristics* section. For females, I expect that sexual abuse frequency will be a prominent factor in relative risk of COD. To show the focal relationship between poverty and COD for females, along with adversities and other covariates, Model 5.5 in Table 5.3 estimates a multinomial logistic regression for disorder outcomes restricted to females in the sample.

Table 5.3 below presents the RRRs just for females for COD relative to no disorder, psychiatric disorder only, and SUD only.

Table 5.3 Multinomial Logistic Regression of COD Outcomes, Females Only (n=19,004)

	Model 5.5: Co-occurring Disorder Risk Relative to:								
	A: No Disorder			B: Psychiatric Disorder Only			C: Substance Use Disorder Only		
Characteristic	RRR		SE	RRR		SE	RRR		SE
Age (years)	0.979	***	0.002	0.980	***	0.002	0.997		0.002
Race (/NH White)									
NH Black	0.477	***	0.046	0.691	***	0.066	0.720	**	0.080
NH Asian	0.661	ǂ	0.119	0.897		0.188	0.641		0.154
Hispanic	0.641	***	0.058	0.905		0.090	0.933		0.108
US-Born (/foreign born)	2.656	***	0.306	2.153	***	0.270	1.302		0.226
Childhood family structure (/two biological parents)									
Reconstituted families	1.028		0.084	0.988		0.083	0.798	ǂ	0.085
Single parent	0.931		0.074	0.922		0.077	0.780	ǂ	0.090
Other	1.507	ǂ	0.293	1.114		0.237	1.183		0.263
Family support (/no)	1.220	**	0.083	1.127		0.083	0.930		0.094
Family history variables									
Family history COD (/no COD)	2.823	***	0.214	1.564	***	0.116	1.874	***	0.200
Family history unknown (/known)	1.461	ǂ	0.254	0.861		0.146	1.221		0.255
Family history SUD (/no SUD)	1.488	***	0.137	1.318	**	0.123	0.967		0.113
Family history psychiatric disorder (/no psych disorder)	2.815	***	0.195	0.977		0.063	2.073	***	0.179
Age at first substance use	0.830	***	0.011	0.834	***	0.011	0.963		0.014
Childhood Poverty (/no)	0.977		0.079	0.907		0.079	0.947	**	0.091
Childhood Adversity Variables									
Childhood Adversities (Count)	1.072	***	0.015	1.037	**	0.013	1.045	ǂ	0.022
Early Sexual Abuse (Freq)	1.643	***	0.128	1.006		0.055	1.484	***	0.130
Early Physical Abuse (Freq)	1.427	***	0.086	1.080		0.054	1.318	**	0.111
Model Statistics: Design df = 113, F (54, 60) = 55.53, p <0.001									

Note: Model is estimated with each comparison relative to COD as the reference group, RRR are re-parameterized to show COD relative to the comparison outcome.

SE = robust standard error, RRR = relative risk ratio, / = omitted reference category

ǂ p<.05; ** p<.01; *** p<.001, Analytic significance level is set to p=0.01 to account for multiple comparisons

5.3.1 COD Relative to No Disorder for Females

I now review the findings for each COD comparison, beginning with COD relative to no disorder, in the same way done for the males. This shows the most extreme comparison of outcomes: predicted probability of COD relative to having no disorder. This comparison illustrates the factors that have associations with COD relative to psychologically healthy females.

In terms of the childhood experience variables, for COD relative to no disorder, the experience of childhood poverty does not change the likelihood of COD for females. Increases in the number of adversities females are exposed to are associated with increased probability of COD as an outcome: with each adversity experienced, the relative risk of COD increases by 7.2% (RRR 1.072, $t=5.04$, $p<0.001$). Sexual abuse frequency and physical/verbal abuse frequency are both associated with increased relative risk of COD too, while controlling for the number of events. Age of first substance use is associated with COD for females: the younger females are when they first use substances, the higher their risk of COD relative to no disorder.

Demographic factors are important to consider because significant differences are seen in many of the variables modelled. Racial/ethnic differences are seen between all groups except Asian Americans for COD vs. no disorder. Hispanics are two-thirds as likely as Whites and Blacks are only half as likely as Whites to have COD: both of these representing large reductions in relative risk. Age is negatively associated, while being a female born in the US is positively associated with COD risk.

Several of the familial characteristics are strongly associated with COD for females. Each type of family history is associated with higher relative risk of COD than no disorder, with COD in a biological parent (RRR =2.823, $t= 13.69$, $p<0.001$), and psychiatric disorder in a parent

(RRR=2.815, t= 14.91, p<0.001) both having large associations. SUD in a parent was also associated with COD, but to a lesser extent, with a smaller relative risk ratio (RRR= 1.488 t=4.32, p<0.001). Family support is significant here for the first time in any of the models estimated and the presence of family support before age 18 unexpectedly increases likelihood of COD, when it would typically be expected to decrease it. Childhood family structure is not associated with COD risk relative to no disorder. The RRR's, robust standard errors, and significance levels for the trends reported here are provided in Table 5.3 above.

5.3.2 COD Relative to Psychiatric Disorder Only for Females

Comparing the relative risk of developing psychiatric disorder in conjunction with SUD (i.e. COD) to just the development of psychiatric disorder is of interest because one is a much more common outcome than the other for females, and this comparison may offer insight into the factors that distinguish the outcome of COD from the more typical outcome of just developing a psychiatric disorder.

The experiences females have in childhood are of mixed relevance to their relative risk of COD vs psychiatric disorder. Poverty does not make a significant difference for females in differentiating COD from psychiatric disorder, and neither does frequency of sexual or physical/verbal abuse. The count of childhood adversities is significant, though not very substantial: for each additional stressor in childhood, the relative risk for the outcome of COD compared to psychiatric disorder increases by a small 3.7% (RRR = 1.037, t=3.01, p=0.003). Only one other childhood experience is significantly associated with COD: age of first substance use increases relative risk of COD compared to psychiatric disorder.

Demographically, age is negatively associated with COD risk for females and being born in the US is again positively associated with COD. Black females are 69.1% as likely as White

females to have COD (RRR= 0.691, t=-3.85, p<0.001) relative to psychiatric disorder, and no other race/ethnicity differences are visible.

From the familial environment, the family history of SUD increases the relative risk of COD, as does family history of COD, but family history of psychiatric disorder is not significant in differentiating co-occurring from psychiatric disorder outcomes. No other family characteristics are significant.

5.3.3 COD Relative to SUD Only for Females

Childhood poverty matters in the difference between acquiring COD and SUD only: females who grow up in households receiving government assistance are less likely to have COD as an outcome than SUD (RRR=0.947, t=-0.57, p=0.573). Referring again to Table 5.3, frequency of physical/verbal abuse and sexual abuse are associated with higher relative risk of COD than SUD but the count of adversities does not differentiate COD from SUD for females in this model, net of the other adversity measures and covariates.

Few demographic variables are significant in comparison 'C' in this model. It is only Black females who are less likely to have COD than White females after adjusting for covariates. No age differences are seen between those who have SUD and COD, net of other variables in the model.

As was the case when COD for females was compared to no disorder, psychiatric disorder in a biological parent is associated with a large increase in COD vs. SUD only, and COD in a parent is also both large and statistically significant for this comparison.

5.3.4 Trends in Factors Associated with Relative Risk Ratios of COD for Females

To aid in synthesis of the information presented for each disorder comparison, I offer a summary of the overall trends in the results for females. In doing so, I highlight variables that

show interesting results and similarities and differences across the outcomes. Occasionally, I comment on whether the males and females showed similar trends, but this is not an indication that I am attempting to compare or test the differences or similarities between these groups post-stratification.

In terms of the childhood experience variable, the experience of childhood poverty does not change the likelihood of COD for females overall (as determined by a post-estimation Adjusted Wald test for poverty and all disorder possibilities, $F(3,111) = 0.51$, $p=0.678$), although it is associated with a significant difference between COD and SUD: where poverty is associated with a decreased likelihood of COD. For the males, poverty was also only significant with the COD vs. SUD comparison, but it was operating in the opposite direction, with the relative risk of poverty being associated with an increased likelihood of COD.

The count of childhood adversities is important to two of the three comparisons made for females. As was true for males, the abuse frequency variables are non-significant net of other variables when comparing COD to psychiatric disorder only for females. Both frequency of abuse variables are significant in COD vs. no disorder and COD vs. SUD only for females.

Also in the grouping of variables representing childhood experiences, age of first substance use is associated with COD relative to psychiatric and no disorder outcomes: the younger females are when they first use substances, the higher their risk of COD relative to each of these two comparisons. Age of first substance use for males was positively associated with COD relative to all three comparisons.

On the whole, childhood family structure and childhood family support are not associated with differences in disorder, although family support appears to play a detrimental role in one

comparison. Family support apparently increases COD risk relative to no disorder. This is discussed in Chapter 7.

Family history variables play a significant role in their association with COD risk for females both because of the magnitude of the associations they bring, and also the statistical significance in their associations with COD for the comparisons made in this section. The associations between family history of disorder and COD follow identical trends to the associations seen for males, with the exception of the variable for family history being unknown.

5.4 Conditional Relationships by Race/Ethnicity

After describing the gender differences in the relationships of interest for this study, I turn next to examine the possibility that these relationships also operate different based on race/ethnicity: a status characteristic that is key to my conceptualization of the impact of stress on COD. Based on the differential access to religious, friend, and familial support networks described in Chapters 1 and 2 for Blacks, Whites, Hispanics, and Asian Americans, I expect that these racial/ethnic groups will be differentially impacted by childhood poverty and adversity and the toll of each of these experiences on COD. I examine this possibility with a series of conditional race/ethnicity multinomial logistic regression models.

5.4.1 Count of Adversities Conditional on Race/Ethnicity for COD

Conditional relationships by race/ethnicity are examined first in the whole sample, and then in the gender-stratified models to test Hypothesis 1b1. I first test the hypothesis that childhood adversities will affect COD differently by racial/ethnic group by introducing the interaction term childhood adversities count × race/ethnicity into a multinomial logistic regression of COD with no other conditional relationships and the full set of covariates,

childhood poverty, and childhood adversity variables, to create Model 5.6a. A post-estimation Adjusted Wald Test for the interaction term in Model 5.6a yielded values of F (9,105) = 2.12 and p= 0.034 (model not shown), providing no evidence at the conservative p<0.01 value used in this dissertation that the association between count of childhood adversities and COD differs by race/ethnicity for the whole population.

Since the test for a conditional relationship between gender and childhood adversity count in Model 5.1a indicated that the count of adversity variable is operating differently for males and females, and the models were ultimately stratified by gender, I further test whether a conditional relationship between childhood adversities count and race/ethnicity is operating in the gender stratified models. Doing this means that although I see the count of childhood adversities is not functioning differently by race/ethnicity in the development of COD for the entire population (because of the non-significant interaction term in Model 5.6a), I think it is possible that this relationship could be significant just for males or just for females in the population. When looking only at disorder outcomes for males, with the term childhood adversities count × race/ethnicity added into Model 5.4 there is no evidence of a conditional race/ethnicity relationship for adversities and COD (post-estimation Adjusted Wald Test F (9, 105) = 1.80, p= 0.076, model not shown). The same is true for females, when the term childhood adversities count × race/ethnicity is added into Model 5.5, there is no evidence of a conditional race/ethnicity relationship (post-estimation Adjusted Wald Test F (9, 105) = 1.41, p= 0.057, model not shown).

5.4.2 Type of Adversity Conditional on Race/Ethnicity for COD

I establish above that the association between count of childhood adversities and COD does not differ by race/ethnicity, but this does not provide information about whether the

associations between frequency of physical/verbal and frequency of sexual abuse with COD differ by race/ethnicity. To additionally assess whether different types of adversity matter differently for racial/ethnic groups, a phenomenon I suspect according to Hypothesis 1b1, two models are estimated each with an interaction term between race/ethnicity and the two frequency measures in the same way that was done for gender. This creates two new models: Models 5.6b and 5.6c (equations provided in Table 3.3). The conditional relationships between frequency of physical/verbal abuse events × race/ethnicity, and frequency of sexual abuse events × race/ethnicity, were both not significant (as indicated by Adjusted Wald Tests for the interaction terms: $F(9, 105) = 3.34$, $p=0.022$; $F(9, 105)= 1.27$, $p=0.287$, respectively).

Collectively, the tests presented here that examine conditional relationships between race/ethnicity and adversity support the rejection of Hypothesis 1b1: different types of childhood stressors do not appear to affect COD differently by racial/ethnic group, and there is no evidence that either measure of frequency of abuse is more strongly associated with COD in Whites than other racial/ethnic groups.

5.4.3 Childhood Poverty Conditional on Race/Ethnicity for COD

Now that it is clear that the manner in which adversity impacts COD is similar regardless of one's race/ethnicity, I investigate the possibility that poverty is operating differently in the way it is associated with COD for racial/ethnic groups in the population. Hypothesis 1b2 asserts that childhood poverty will affect COD differently by racial/ethnic group, with childhood poverty being more strongly associated with COD in Whites compared to all other racial/ethnic groups. To test this hypothesis, I introduce a term that is the product interaction of childhood poverty × race/ethnicity to a multinomial logistic regression with the full set of covariates, childhood poverty, and childhood adversity variables, with the whole sample: creating a new

model, Model 5.7. This conditional relationship was not significant (post-estimation Adjusted Wald Test F (9, 105) = 1.28, p= 0. 256, model not shown).

As was done in *Section 5.4.1* with the conditional adversity relationships, the conditional poverty and race/ethnicity relationships are tested in the gender stratified models (Models 5.4 and 5.5) as well, to examine the possibility that the conditional race/ethnicity relationship exists *only* for males, or *only* for females. When looking only at disorder outcomes for males, with the term childhood poverty × race/ethnicity added into Model 5.4 there is no evidence of a conditional race/ethnicity relationship for poverty and COD (post-estimation Adjusted Wald Test F (9, 105) = 1.07, p= 0.393, model not shown). For females, when the interaction term childhood poverty × race/ethnicity was added to a multinomial logistic regression of disorder outcomes (Model 5.5), a post-estimation Adjusted Wald test showed that this product interaction term was not significant (F (9, 105) = 2.02, p= 0.044). Thus, there is no evidence that the association between childhood poverty and COD differs by race/ethnicity.

5.5 Childhood Poverty Conditional on Childhood Adversity

5.5.1 *Childhood Poverty Conditional on Adversity for COD*

Aim 2 of this dissertation tests whether the association between childhood poverty and COD lifetime occurrence is intensified by the number of childhood adversities experienced, by the frequency of adversity (for sexual and physical/verbal abuse) and if that conditional relationship differs by race/ethnicity and gender. There are a multitude of conditional relationships hypothesized here, and I summarize the models and their findings (with respect to the significance of the product interaction terms introduced) in Table 5.4.

Table 5.4 below displays all of the interactions tested for Aim 2. Model numbers, the product interaction terms tested, the post-estimation Adjusted Wald Test statistic, and the p-value for the interaction term.

Table 5.4. Summary of Conditional Relationships Tested for Aim 2 of the Dissertation

Model Number	Product interaction term tested	Base Model Interaction is Added to	Post-estimation Adjusted Wald Test Statistics	P value for the interaction term
Model 5.8a	Childhood Poverty × Childhood Adversity Count	Model 4.3 (main effects)	F(3,111) = 0.45	p= 0.717
Model 5.8b	Childhood Poverty × Frequency of Sexual Abuse	Model 4.3 (main effects)	F(3,111) = 1.46	p= 0.228
Model 5.8c	Childhood Poverty × Frequency of Physical/Verbal Abuse	Model 4.3 (main effects)	F(3,111) = 0.87	p= 0.457
Model 5.9a	Childhood Poverty × Childhood Adversity Count × Race/ethnicity	Model 4.3 (main effects)	F(9,105) = 1.89	p= 0.062
Model 5.9b	Childhood Poverty × Frequency of Sexual Abuse × Race/ethnicity	Model 4.3 (main effects)	F(9,105) = 0.69	p= 0.714
Model 5.9c	Childhood Poverty × Frequency of Physical/Verbal Abuse × Race/ethnicity	Model 4.3 (main effects)	F(9,105) = 0.72	p= 0.689
Model 5.10a	Childhood Poverty × Childhood Adversity Count × Gender	Model 4.3 (main effects)	F(3,111) = 0.91	p= 0.441
Model 5.10b	Childhood Poverty × Frequency of Sexual Abuse × Gender	Model 4.3 (main effects)	F(3,111) = 0.76	p= 0.519
Model 5.10c	Childhood Poverty × Frequency of Physical/Verbal × Gender	Model 4.3 (main effects)	F(3,111)= 1.26	p= 0.292

To test if the impact of childhood poverty on the likelihood of developing lifetime COD is intensified or subdued by number of childhood adversities, the interaction term of these two variables is first added to a multinomial logistic regression with the full set of covariates, childhood poverty, and childhood adversity variables, a multinomial logistic regression with no other conditional relationships with the whole sample. The term is not statistically significant (as can be seen in the first row of Table 5.4, Model 5.8a) and there is no evidence of the effect of poverty being conditional on number of adversities. It could still be the case that it is not number of adversities but rather the frequency of certain types of adversities that is moderating the relationship between poverty and COD. I go on to test this possibility through two models

(Model 5.8b and 5.8c) by introducing product interaction terms for childhood poverty × frequency of sexual abuse and childhood poverty × frequency of physical/verbal abuse into two separate models, each with the full set of covariates, childhood poverty, and childhood adversity variables. Both of these product interaction terms are non-significant.

The hypotheses for this Aim posited that the conditional relationship of childhood poverty and childhood adversities would differ by race/ethnicity and also by gender. For the whole population, the three-way interaction term of childhood poverty × count of childhood adversities × gender along with associated lower order terms were added to the models to test this, however, this interaction was not significant as can be seen in Table 5.4 for Model 5.10a (post-estimation Adjusted Wald Test F (3,111) = 0.91, p= 0.441). As with the set of interactions in the previous paragraph, I again test whether frequency of sexual abuse and physical/verbal abuse are playing a role in the hypothesized conditional relationships related to poverty and adversity. I do this by introducing product interaction terms for childhood poverty × frequency of sexual abuse ×gender and childhood poverty × frequency of physical/verbal abuse × gender and their associated lower-order terms into two separate models (Models 5.10b and 5.10c), each with the full set of covariates, childhood poverty, and childhood adversity variables. Both of these product interaction terms are non-significant indicating that the relationship between childhood poverty and childhood adversity is not conditional on gender, with respect to COD.

For the last set of conditional relationships tested in Aim 2, I examine the possibility that the conditional relationship between poverty and adversity is moderated by race/ethnicity. I suspect this could the case because of the confluence of stress related to discrimination and early social circumstances for racial/ethnic minorities and the potential for these stressors to behave in synergistic ways under those circumstances. Following the pattern of the results discussed above,

I test three models here: each with a different three-way product interaction term in it. I do this to test the conditional relationship between childhood poverty, adversity, and race/ethnicity using the three different variables related to adversity. First, I introduce an interaction term for childhood poverty × count of childhood adversities × race/ethnicity into a model with the full set of covariates, childhood poverty, and childhood adversity variables, this creates Model 5.9a. I include the associated lower-order terms, and the non-significant p-value for the product interaction term in Model 5.9a indicates that there is no three-way conditional childhood poverty and count of childhood adversities and race/ethnicity. I do this two more times, with the frequency of adversity variables, first introducing the product interaction term childhood poverty × frequency of sexual abuse × race/ethnicity (and associated lower-order terms) into a new model with the full set of covariates, childhood poverty, and childhood adversity variables, creating Model 5.9b; and then introducing the product interaction term childhood poverty × frequency of physical/verbal abuse × race/ethnicity (and associated lower-order terms) into another new model, Model 5.9c. Neither one of the type of abuse variables were significant, showing that the relationship between childhood poverty and adversity is not additionally conditional on race/ethnicity. As such, irrespective of the way it is measured here, there does not appear to be a significant three-way relationship between poverty, adversity, and race/ethnicity. Non-significant models are not shown.

Therefore, I conclude that there are no conditional childhood poverty and childhood adversity relationships of the ones I tested, even considering the possibility of their further moderation by gender and race/ethnicity.

5.6 Sensitivity Testing with Alternative COD Definition

In this section, I briefly assess the extent to which the conclusions drawn about the focal relationship from Aim 1 would still be similar if a definition of COD that accounted for temporal overlap of disorders was used instead of the lifetime definition I use in this dissertation. Specifically, COD was alternatively defined as temporally overlapping psychiatric disorder and SUD in the year prior to data collection. This definition applies a more restrictive analysis that is more closely aligned with the definition used in clinical research. This variable contains four possible categories: "recent COD," "recent psychiatric disorder only," "recent SUD only," and "no recent disorder." I run multinomial logistic regression models testing only the significant product interaction terms (and all covariates) from Model 5.3 in Aim 1 using the definition of temporal COD overlap instead of lifetime COD. Using the dependent variable of overlapping COD in the past year, I find that a model that includes product interaction terms for both childhood poverty × gender and count of childhood adversities × gender shows statistically significant interactions between gender and these two childhood variables (post-estimation Adjusted Wald test values of $F(3,111) = 4.48$, $p=0.005$; and $F(3,111) = 9.37$, $p<0.001$, respectively). Although the samples and models are different with these two COD definitions, the conclusions drawn about the moderation of childhood poverty and adversities by gender would be similar.

5.7 Chapter Summary

Chapter 5 examined conditional relationships between childhood poverty and disorder as well as childhood adversity and disorder. Significant interaction terms for childhood poverty × gender as well as childhood adversity count × gender indicated that the antecedents of lifetime

disorder co-occurrence are operating differentially for males and females, and gender-stratified analyses were presented to aid in interpretation of these differences, and because disorder development is likely operating in different ways for males and females. No other conditional relationships were found, including the ones tested with race/ethnicity and the conditional relationships examined between poverty and adversity. This indicates that poverty and adversity are functioning in similar ways across racial/ethnic groups in the way they are impacting COD. The various non-significant interactions for childhood poverty and adversity terms are telling: despite my expectations that these material and social stressors would act synergistically together, they did not, and the effects of poverty on COD and adversity on COD are independent.

CHAPTER 6:

TIMING OF DISORDERS OVER THE LIFE COURSE

Chapter 6 builds on the relationships examined in Chapters 4 and 5 by adding a temporal component to the analyses of childhood poverty, childhood stressors, and onset of disorders. This chapter begins with a description of the univariate age of onset of substance use and psychiatric disorders. Then, I describe the survival analysis done using a Cox Proportional Hazard Model with the whole population and time to second disorder for those who develop COD. Within this analysis I show that demographics, family history, and childhood adversity are important factors in studying disorder onset. The sample for the analysis then is limited to a Cox Proportional Hazard Model for only those who develop at least one disorder, so that sequence of disorders can be studied. Here, the model estimates time to second disorder for those who already have a psychiatric disorder or SUD, and this model accounts for the sequence of developing COD, for those who go on to develop it. Testing the conditional relationship between gender and disorder sequence, I find a significant difference in the impact of the type of disorder on COD by gender. The analyses conclude with two stratified models looking at risk factors associated with COD for those who have SUD distinctly from risk factors for COD for those who have psychiatric disorders in separate Cox models.

6.1 Age of Onset of Individual Disorders

6.1.1 Age of Onset of Specific Psychiatric and Substance Use Disorders in the Population

This chapter begins by looking at the age of onset of individual disorders, and then the two types of disorders, so that age of onset of COD (a measure composed of the onset of two

separate disorder types), can be better understood. Looking at the age of onset of disorders and their distribution in the population is important to capture before a composite measure (like age of onset of COD) is introduced because it gives information about the variation in age of onset of the components of COD, and indicates how wide the window is in which people get their first disorders according to type of disorder. See the mean onset of specific disorders in Table 6.1 below. Table 6.1 shows the number of people in the sample who developed each disorder (or disorder type) in the first column, the weighted mean age of onset for those who developed the disorder in the second column, and the standard deviation around the mean for each disorder.

As shown in Table 6.1, there is substantial variation within these categories, for example, within SUD, marijuana use disorder has a mean onset between ages 21-22 while the much less common sedative use disorder onsets between 27-28 on average. Alcohol use disorder typically occurs for the first time at a mean age of 26.136 (with a standard deviation of 10.901 indicating that there is wide dispersion in the population from the mean value). All of the mean ages of onset for SUD fall in the 20's, which aligns with the histogram shown in Figure 6.1, and indicates that people are, on average, young adults when they develop a disorder with a substance for the first time. Within psychiatric disorders, there is even more dramatic variation than is seen with the mean age of onset for SUD. Table 6.1 shows that conduct and antisocial disorders have a mean onset of nearly 12 years old (with relatively little variation in the age of onset, indicated by a standard deviation of 2.414), and specific and social phobias also onset early (close to 14 and 16 years old, respectively). The phobias have dispersion around the mean that is very wide, as can be seen in the standard deviations for these disorders from Table 6.1, showing that although the mean values are 14.111 and 16.517, many people in the population have ages of onset for specific phobia and social phobia that deviate substantially from these

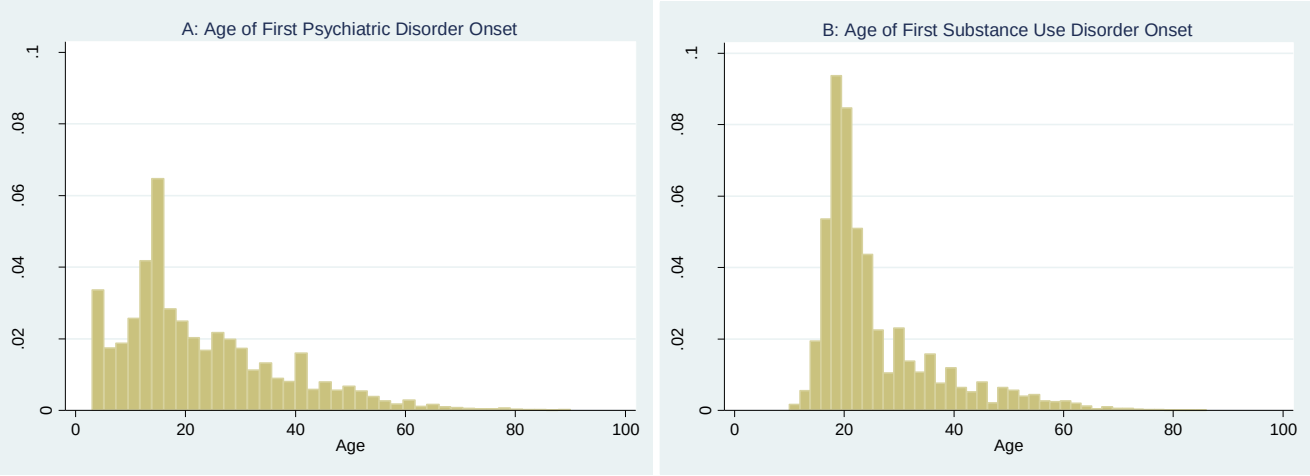
values. In contrast, the age of onset of major depressive disorder and generalized anxiety disorder are well into early adulthood (29 and 31, respectively). Generalized anxiety disorder has the latest age of onset of all of the disorders at 31.134, and there is a standard deviation of 15.361 for this value. The mean onset for each disorder as well as for categories of disorders (e.g., internalizing disorder) and types of disorder (e.g., psychiatric disorder) are given in Table 6.1 There is wide variation in the means for each disorder onset shown in Table 6.1, as indicated by the large standard deviations.

Table 6.1. Mean Age of Onset of Specific Psychiatric and Substance Use Disorders

	Unweighted N	Weighted Mean	Standard Deviation
Total	33,767	N/A	N/A
Any Substance use disorder	10,715	25.298	10.833
Alcohol use disorder	9,834	26.136	10.901
Any Drug use disorder	3,415	23.290	9.559
Marijuana use disorder	2,214	21.552	9.219
Cocaine use disorder	851	24.741	7.814
Stimulant use disorder	558	23.155	7.914
Sedative use disorder	353	27.416	13.808
Any Psychiatric disorder	12,523	22.684	14.479
Any Internalizing disorder	11,352	24.517	14.686
Major depressive disorder	7,315	29.056	14.113
Dysthymia	2,256	28.348	14.503
Panic disorder	1,772	28.204	12.498
Social phobia	1,239	16.517	10.891
Specific phobia	2,236	14.411	11.045
Generalized anxiety disorder	2,661	31.134	15.361
Agoraphobia	679	23.086	12.464
Mania	993	24.107	11.767
Any Externalizing disorder (conduct or antisocial disorder)	1,573	11.943	2.414
Any Eating disorder	583	21.541	9.901
Anorexia nervosa	257	19.001	6.324
Bulimia nervosa	348	23.512	12.046
Any Post-traumatic stress disorder	2293	23.857	14.072

On average, people tend to develop psychiatric disorders earlier in their lives than they develop SUD. The mean age of onset for all psychiatric disorders is not quite 23 years old, while the mean for all SUD is over 25 years. The histograms in Figure 6.1, which show the age of onset for everyone who had a psychiatric or SUD in the sample, illustrate this difference in the mean age at which people develop each type of disorder. The histogram for age of onset for first psychiatric disorder (for those who have this type of disorder) shows earlier onset and is spread more widely than the mean age of onset for SUD curve, which has a tall peak surrounding age 20. Because the distribution of values for age of onset for the disorders is so wide, the mean values should be interpreted with caution, as many people have onsets substantially earlier or later, a trend that can be visually seen in Figure 6.1.

Figure 6.1 Histograms of Age of Onset of First Psychiatric Disorder and Age of Onset of First SUD



6.1.2 Age of Onset of Types of Disorder for Those With and Without COD

Research suggests that individuals with COD have earlier onset of disorders, on average (Najt et al., 2011), relative to individuals with a single disorder type, and thus it is valuable to look at onset of disorders for those who go on to develop COD. I assess how age of onset differs

for those with COD from those with only one disorder by the time of interview, at a bivariate level. For everyone with lifetime COD, age of onset of first psychiatric disorder is just under 20 years old (19.700), on average, while mean onset of their first SUD is just over 24 (24.310). These ages are notably younger than the means for those with only one disorder, which are 25.207 for psychiatric disorder and 26.402 for SUD. I test the statistical significance of this difference in age of onset between those with COD and those with only one disorder type using the Adjusted Wald test ($F(1,113) = 299.52$, $p<0.001$, and $F(1,113) = 51.74$, $p<0.001$, respectively).

Onset of a second type of disorder may be impacted by the type of disorder that a person develops first (Najt et al., 2011). This is necessary to investigate at a bivariate level before proceeding to multivariate analyses. In this sample, there are bivariate differences between age of onset for those who had psychiatric disorder compared to SUD first, among those with co-occurrence. These differences and the Adjusted Wald tests that determine the statistical significance of these differences are given in Table 6.2 below and discussed after the table in the text.

Table 6.2. Mean Age of Onset of Types of Disorders based on Disorder Sequence for Those with COD

	Unweighted N	Weighted Mean	Standard Deviation
Total			
Co-occurring disorder	N/A	N/A	N/A
Psychiatric Disorder (if psychiatric first)	3,926	14.245	8.107
Psychiatric Disorder (if SUD first)	1,834	32.524	11.133
F-test (Adjusted Wald test)[1]	F (1,113) = 2196.86, p<0.001		
SUD (if psychiatric first)	3,926	25.611	11.453
SUD (if SUD first)	1,834	21.001	8.395
F-test (Adjusted Wald test)[2]	F (1,113) = 200.30, p<0.001		
Onset (SUD and psychiatric simultaneous)	398	24.193	9.321

Note: NA = not applicable, Means are weighted
[1] Testing difference in mean psychiatric disorder onset for those with COD who had psychiatric disorder onset first vs. SUD onset first
[2] Testing difference in mean SUD onset for those with COD who had psychiatric disorder onset first vs. SUD onset first

On average, those with COD who develop SUD first have it onset in their early 20's and then have their average psychiatric disorder onset in their early 30's, as Table 6.2 indicates, although the standard deviations are large and show that there is a large amount of variation in the average age of onset. For those with COD who develop psychiatric disorder first, onset happens much earlier, in adolescence, on average, and their development of SUD occurs in the mid-twenties, again, this deviated from the mean by a standard deviation of 8.107 for the psychiatric disorder onset and 11.453 for SUD onset. These differences are statistically significant, as shown in the F-tests in Table 6.2. For those who have both disorders onset within the same year, the mean age of onset of COD is 24 years old.

6.2 Co-occurring Disorder Hazard Whole Sample

Aim 3 of the dissertation is to estimate the association between experiencing poverty and different types of stress in childhood and the timing of developing COD. The results from the analyses for Aim 3 are given in this chapter using time-to-event data. The dependent variable for

the Aim 3 analyses is the age at which respondents develop their second disorder (for those who have two). For the analyses presented here in Section 6.2, the time period studied is the period from birth until someone develops a COD, marked by the age at which they develop their second type of disorder. For the preliminary analysis for this Aim, I assess the proportionality of predictors in the model and their associations with time to COD. The timing of COD in this Aim is estimated through a series of Cox Proportional Hazard models.

6.2.1 Survival Curve and Hazard Function for COD without Covariates

The survival and smoothed hazard curves for the development of COD over the life span depicted in Figure 6.2 can be used to describe risk over time for co-occurrence. I first examine the baseline hazard function and the baseline survival curve to understand the trends related to onset of COD over the life course, without adjustment for demographics, family characteristics, and childhood experiences. The survival analysis here models COD risk over time, with the failure in the model being the development of the second disorder. In this time-to-event model that includes the whole sample, someone is at risk for COD from birth until the age they develop COD or until the age at which they are interviewed for NESARC-III and hence censored. The failure variable in this model is a binary variable that captures lifetime COD (Yes=1/ No=0), and the model accounts for the time between the starting period (birth) and the determination of the outcome. For those who have not developed COD by the time they are interviewed, they are at risk for the entire duration of the study and their observation is censored at the age of interview. Note that this model by design groups together all other outcomes in the "no lifetime COD" group including those with no disorder, those with psychiatric disorder only, and those with SUD only, for reasons discussed in detail in Chapter 3, *Section 3.9.4*. Briefly, these disorders were grouped together because the Cox Proportional Hazard Model only handles models with one

failure, and is not able to account for the "failure" event of a first disorder distinctly from a second disorder. Multiple failure models like the Conditional Risk Set Model were considered but ultimately were not selected for use in the study because they constrain the effect of covariates to be the same across all failure types.

Figure 6.2 Survival Curve and Hazard Function for COD, Whole Sample

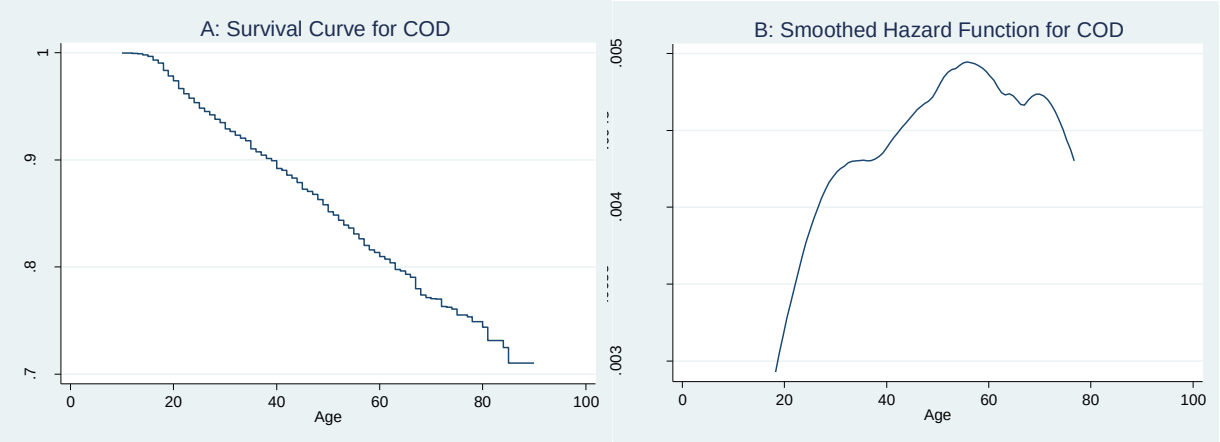


Figure 6.2 curves are derived from models estimated using a Cox Proportional Hazard Model with no covariates. The Cox model used here does not constrain the shape of the hazard being modelled. The survival curve for COD generated from this model shows cumulative survival of the population over time. This curve decreases in a linear manner, steadily over time showing no obvious periods of accelerated risk. There is almost no risk before the age of 18 with a survival of 1.0, and by age 90 the survival without COD is approaching 0.7. The smoothed hazard function, which shows the instantaneous rate of occurrence of COD given that one has not already developed COD, is more instructive in determining the risk periods throughout the life course. The hazard increases sharply in the 20's and between ages 30-40 there is a leveling off of the hazard function for COD. After age 40 and until about age 55, the hazard function again increases for those who have not yet developed COD, although the slope of the function

appears not as steep as it was between ages 20-30. The hazard function peaks at age 60, and decreases after that until the end of life. In summary, the periods of greatest risk for COD onset appear to be in early adulthood and then again in very late middle age as people approach retirement age (for those who did not already develop COD).

6.2.2 Model Building and Assessment of Proportionality for Model 6.1

Before adding covariates into the Cox model described here, two important steps were taken (as described in Chapter 3's *Preliminary Analysis for Survival Analysis* section): 1) equality of the survival function was estimated using the logrank test in Stata for each categorical covariate under consideration to determine whether to include it in the models, and 2) the proportionality of covariates was tested to address any violations of the proportional hazard assumption. Significant values seen for the logrank test indicate variables that are significantly associated with COD risk over time and these are variables that will be considered for inclusion in the models. Significant values for the Schoenfeld residual test indicate variables that violate the assumption of proportionality of effects over time. Both of these tests were conducted to ensure that the multivariate survival analysis planned was statistically sound.

The logrank test yielded significant values for all covariates under consideration: race, gender, nativity status, family support, family history of psychiatric disorder, family history of SUD, family history of COD, family composition, and childhood poverty. Thus, the categorical covariates tested above were included along with the continuous variables for age, childhood adversity count, sexual abuse frequency and physical/verbal abuse frequency in the models.

When the proportionality of covariates was tested using the Schoenfeld residual test as obtained through the 'estat phtest, detail' command in Stata, most covariates did not violate the

assumption of proportionality over time. However, race/ethnicity (specifically Blacks and Hispanics), age and the childhood adversity count variable violated the assumption. This suggests that the risk of COD according to race/ethnicity, age, and childhood adversity count is not proportional over time. There are several ways to accommodate this violation of the model assumption, and I consider two options: 1) assessing the variation over time to determine if it is necessary to make an adjustment or if it can be ignored, and 2) including the variables as time-varying coefficients in the model to adjust for this violation (this option interacts the variables with a function of time to allow the effect over time to vary).

Considering the first option, the largest variation in effect over time is seen with the covariate for age, where the time varying-effect is 0.999. Multiplied by the 90-year time period under study in this model, the effect of age varies a maximum of <2% over the entire sample and this is considered negligible enough to ignore in the models (Cleves, 2008). Based on similar calculations, race/ethnicity and the childhood adversity variable also vary by less than 2%. The other alternative for dealing with the violation of proportionality that I consider is the inclusion of the violating variables as time-varying coefficients in the models. Including these variables and interacting their effects with time does not change the results of the models in a substantive way (see Appendix B for a comparison of the models with and without time-varying effects accounted for). Using the time-varying coefficients addresses the assumption of proportionality, however, it does not allow the use of sample weights and survey variables, and it does not allow for the generation of survival curves. Thus, the violation of proportionality seen for these models will be ignored because the variation in the effect is sufficiently small and accounting for it does not make a substantively meaningful difference in the final results.

6.3 Childhood Poverty, Childhood Adversity, and COD Hazard Over Time

To study childhood poverty, childhood adversity, and COD risk in the survival models, I start the analysis with the bivariate relationships between these childhood variables and onset of COD through two bivariate Cox Proportional Hazard Models. After the bivariate associations are described, I examine the multivariate associations. To test Hypotheses 3a, that childhood poverty will be associated with increased risk of COD over the life course, and to test Hypothesis 3b that childhood stressors will be associated with increased risk of COD over the life course, Model 6.1 is estimated. Model 6.1 tests the associations between the focal independent variable and COD in the entire sample using a Cox Proportional Hazard model with the clock starting at birth and time to second disorder as the outcome, net of other explanations and controlling for covariates (including demographics, family characteristics, and childhood experiences).

6.3.1 The Association of Childhood Poverty with COD Over Time

The zero-order association between childhood poverty and risk of having COD over the life course is estimated with the Cox Proportional Hazard model. Persons with a history of childhood poverty have a substantially higher rate of developing COD than those without that history across the entire interval. The bivariate hazard ratio is 2.405 (SE = 0.096, $p < 0.001$, bivariate model not shown), which means that persons exposed to childhood poverty have a 140.5% greater risk of developing COD than those not exposed.

When alternative explanations are accounted for with other covariates included (as seen in Model 6.1, Table 6.3), this hazard ratio is only 1.096 (SE = 0.047, p=0.064) and is not statistically significant meaning that controlling for covariates, having poverty in childhood is not associated with the development of COD net of other explanations (as seen in Model 6.1, Table 6.3). The association disappears with the addition of the childhood adversity variables,

specifically. Although I was not able to formally test mediation, I expect that some of the variables I have included are operating as mediators of the effects of childhood poverty on COD, including family support, childhood adversity variables, and age of first substance use. Seeing the variable for childhood poverty become non-significant when other alternative explanations are accounted for may indicate that the direct association between childhood poverty and COD is being explained by other variables in the model.

Thus, I can reject the hypothesis that childhood poverty is related to COD over the life span, after accounting for alternative explanations, but I suspect that this lack of association is due to the effects being accounted for by the inclusion of untested mediators in the model.

6.3.2 The Association of Childhood Adversity with COD Over Time

I now shift focus from childhood poverty to childhood adversity with an examination of the adversity variables that are part of Model 6.1 in Table 6.3 below. Being exposed to adversity before the age of 18 is also associated with increased hazard of COD. Each adversity experienced incurs an additional 7.0% hazard relative to no adversities (based on the hazard ratio of 1.070, SE = 0.008, $p<0.001$, as seen in Model 6.1) for every adversity experienced after accounting for all other variables (including frequency of sexual abuse and physical/verbal abuse). Frequency of sexual abuse and frequency of physical and verbal abuse before age 18 are both significantly associated with the development of COD over the life course, net of all other variables (including the childhood adversity count variable).

This significance of the count of adversity variable remains even after including variables that account for the frequency of physical/verbal and sexual abuse. This indicates that both how many adverse experiences people have, in total, in childhood, as well as the frequency with which the most impactful of these experiences happen, are both distinctly important to the

development of COD over time. Childhood sexual abuse and physical/verbal abuse are included in the count as well as the frequency measures, but in different ways. They contribute to the count as overall bad experiences that happen or do not happen to people before the age of 18, while they contribute to frequency variables that captures how often the exposure happened.

Hypothesis 3a1 asserts that childhood stressors will be associated with increased risk of COD over the life course, and that sexual abuse will add additional risk to the hazard incurred by other stressors. Regarding Hypothesis 3a1, I test this through my test of the null hypothesis in Model 6.1 (H0: $\beta_{Cstress} = 0$ or $HR_{Cstress} = 1$) that the number of childhood adversities is not related to COD, net of all other variables, and that sexual abuse frequency is also not associated with increased risk for COD (H0: $\beta_{CSexualAbuse} = 0$ or $HR_{CSexualAbuse} = 1$) as can be seen in Table 6.3. This information is used to fail to reject Hypothesis 3b. Table 6.3 displays the coefficients and standard errors for Model 6.1, the weighted Cox Proportional Hazard model of time to COD with the whole sample.

Table 6.3. Cox Proportional Hazard Model of Lifetime COD Risk, Whole Sample (n=32,635)

	Co-occurring Disorder Hazard		
	Model 6.1		
Characteristic	HR		SE
Age (years)	0.941	***	0.002
Male (/female)	1.246	***	0.049
Race (/NH White)			
NH Black	0.591	***	0.037
NH Asian	0.551	***	0.066
Hispanic	0.757	***	0.041
US-Born (/foreign born)	2.375	***	0.178
Childhood family structure (/two biological parents)			
Reconstituted families	0.987		0.045
Single parent	0.988		0.049
Other	1.220		0.130
Family support (/no)	1.108	ǂ	0.048
Family history variables			
Family history COD (/no COD)	1.874	***	0.071
Family history unknown (/known)	1.251	**	0.117
Family history SUD (/no SUD)	1.410	***	0.079
Family history psychiatric disorder (/no psych disorder)	1.766	***	0.068
Childhood Poverty (/no)	1.096	ǂ	0.047
Childhood Adversity Variables			
Childhood Adversities (Count)	1.070	***	0.008
Early Sexual Abuse (Freq)	1.114	**	0.034
Early Verbal and Physical Abuse (Freq)	1.163	***	0.037

Note: SE = robust standard error, HR = hazard ratio

ǂ p<.05; ** p<.01; *** p<.001, Analytic significance level is set to p=0.01 to account for multiple comparisons

6.3.3 The Association of Other Variables with COD Over Time

This model contains other factors that are associated with COD risk, and the associations of these variables with COD, net of other variables in the model, are shown in Table 6.3. All of the demographic variables are significantly associated with COD: being born in the US brings an associated hazard ratio of 2.375 (SE = 0.178, $p<0.001$), which increases the hazard by 137.5% compared to those who are born elsewhere. Each of the other racial/ethnic groups have a lower hazard of COD than Whites, the most striking difference being for Asian Americans who have a hazard that is about half the hazard of Whites (HR = 0.551, SE = 0.066, $p<0.001$). Blacks and Hispanics also have a lower hazard ratio for COD than Whites. Being male increases COD risk, 24.6% more than being female does. Age is negatively associated with COD.

Having COD in either one's biological mother or father once again is associated with a large increase COD hazard ratio. In the survival analysis, COD in the family history is associated with an 87.4% increase in the hazard ratio of COD, while having psychiatric disorder only in a parent increases the hazard ratio by 76.6% and SUD only by 41.0%. Not knowing your parent's disorder status is also associated with an increase in the hazard ratio for COD (HR = 1.251, SE = 0.117, $p = 0.004$). Family configuration growing up is not significantly associated with COD hazard over the life course net of other variables in the model. The hazard ratios and test statistics corresponding to these findings can be seen in Table 6.3.

6.4 Hazard of Co-occurrence Given One Disorder

Model 6.1 above tested the association between childhood poverty, childhood adversity, and timing of COD onset over the life course (with COD onset being the age at which the second disorder begins) for the entire population. There are additional questions about the development of a second disorder type, after one already has a first disorder type, that cannot be answered within the Cox model from Model 6.1.

Thus, a second set of Cox Proportional Hazard models were estimated, to determine the ability to reject or fail to reject Hypotheses 3d to 3f which concern the rate of co-occurrence after the development of any psychiatric disorder or SUD. This set of analyses was restricted to respondents who had at least one disorder to determine how hazard of COD changes after the development of SUD or a psychiatric disorder. The survival analysis in Model 6.2 models COD hazard over time (relative to only having a single type of disorder over the life course), with the failure in the model being the development of the second disorder. In this time-to-event model that includes only people who have any SUD or psychiatric disorder (Model 6.2 below), someone is at risk for COD from the age they develop their first disorder until the age they develop COD or until the age at which they are interviewed. The failure variable in this model is a binary variable that captures lifetime COD (Yes=1/ No=0), and the model accounts for the time between the starting period (first disorder) and the determination of the outcome. For those who have not developed a second type of disorder by the time they are interviewed, they remain at risk for the entire duration of the study and their observation is censored at the time of interview: modelling age at second disorder beginning from the age of first disorder. Not everyone in this sample goes on to develop COD.

6.4.1 Model Building and Assessment of Proportionality for Model 6.2

As with the Cox Model for the whole sample, Model 6.1 in Table 6.3, preliminary analyses are conducted here to ensure that the models do not violate any of the assumptions of the statistical tests they use. The results of these preliminary analyses are tabled in Appendix C. The logrank test yielded significant values for nearly all covariates under consideration for Model 6.2. Family support was not determined to be statistically significant according to the logrank test, however this variable is included in the model because it is an important theoretical resource for the development of disorder, and it was included in all prior models. Thus, the categorical covariates included were: race/ethnicity, family composition, family history, nativity, gender, and disorder sequence; the continuous variables included were: age, childhood adversity count, sexual abuse frequency and physical/verbal abuse frequency in the final model. The results of the logrank test can be seen in Appendix C.

When the proportionality of covariates was tested using the Schoenfeld residual test as obtained through the 'estat phtest, detail' command in Stata, most covariates did not violate the assumption of proportionality. However, race/ethnicity, gender, and disorder sequence violated the assumption, and therefore were assessed in a similar way to the variables in Model 6.1 that violated the assumption of proportionality. Risk of COD for those with one disorder according to race/ethnicity, gender, and disorder sequence was not proportional over time. First I assess the variation of the residuals of these covariates over time to determine if it is necessary to make an adjustment or if it can be ignored.

The largest variation in effect over time is seen with the covariate for disorder sequence, where the time varying-effect is 1.000, which indicated that the effect of disorder sequence

varies a maximum of <1% over the entire period and this is considered negligible enough to ignore in the models (Cleves, 2008). Race/ethnicity and gender variable also vary by less than 1%. To be sure that ignoring the violation of proportionality does not change the results of the analysis, I include the violating variables as time-varying coefficients in the models and see no substantive differences (see Appendix D for a comparison of the models with and without time-varying effects accounted for). As with Model 6.1, the violation of proportionality seen for these models will be ignored because the variation in the effect is sufficiently small and accounting for it does not make a substantively meaningful difference in the final results.

6.4.2 Childhood Poverty and Childhood Adversity and COD Hazard, Given One Disorder

In Model 6.2 in Table 6.4, which assumes the effects are constant across all the groups in the model, many of the relationships seen in the analyses done with the entire sample parallel those in the survival analysis for those who have at least one disorder, indicating that factors associated with COD risk for people in the general population are not dramatically different from factors associated with COD risk for people who already have a disorder. This convergence is helpful in determining the key characteristics and exposures that are important with COD. These results are displayed in Table 6.4 and are discussed below.

Table 6.4 below shows the hazard ratios, significance levels, and standard errors associated with Model 6.2, a Cox Proportional Hazard model for those with at least one type of disorder, to determine the factors associated with the development of a second type of disorder. Table 6.4 also shows the hazard ratios, significance levels, and standard errors associated with Model 6.6, which builds on Model 6.2 by introducing a product interaction term. Model 6.6 will be discussed in *Section 6.5.*

Table 6.4. Cox Proportional Hazard Models of COD Hazard Given One Disorder, and COD Hazard Given One Disorder with Disorder Sequence Conditional on Gender (n=14,465)

	Co-occurring Disorder Hazard After Experiencing One Disorder					
	Model 6.2 Main Effects Model			**Model 6.6** Disorder Sequence × Gender Interaction		
Characteristic	HR		SE	HR		SE
Age (years)	0.958	***	0.002	0.958	***	0.002
Race (/NH White)						
NH Black	0.778	***	0.043	0.768	***	0.043
NH Asian	0.689	**	0.075	0.681	**	0.074
Hispanic	0.934		0.046	0.919		0.046
US-Born (/foreign born)	1.596	***	0.116	1.581	***	0.116
Childhood family structure (/two biological parents)						
Reconstituted families	0.990		0.044	0.986		0.043
Single parent	0.960		0.050	0.961		0.050
Other	1.004		0.109	0.989		0.105
Family support (/no)	1.067		0.046	1.059		0.043
Family history variables						
Family history COD (/no COD)	1.384	***	0.055	1.358	***	0.055
Family history unknown (/known)	1.105		0.107	1.081		0.106
Family history SUD (/no SUD)	1.256	***	0.071	1.238	***	0.069
Family history psychiatric disorder (/no psych disorder)	1.193	***	0.041	1.182	***	0.042
Childhood Poverty (/no)	1.034		0.046	1.041		0.048
Childhood Adversity Variables						
Childhood Adversities (Count)	1.031	***	0.008	1.029	***	0.008
Early Sexual Abuse (Freq)	0.997		0.029	1.020		0.031
Early Verbal and Physical Abuse (Freq)	1.038		0.030	1.042		0.030
Male (/female)	1.318	***	0.046	0.609	***	0.042
Psychiatric Disorder (/SUD)	1.361	***	0.071	0.752	***	0.044
Psychiatric Disorder × Male	N/A		N/A	2.832	***	0.222

Note: SE = robust standard error, HR = hazard ratio

ǂ p<.05; ** p<.01; *** p<.001, Analytic significance level is set to p=0.01 to account for multiple comparisons

In Model 6.2, those with childhood poverty do not have a substantially higher rate of developing COD than those without it, controlling for covariates and accounting for alternative explanations, in the group of people who already have one disorder.

For the other childhood experience variables, being exposed to adversity before the age of 18 is associated with increased risk of COD for those who have one disorder, but that effect is small, with each adversity increasing the hazard ratio by only 3.1% (SE = 0.008, $p<0.001$). Sexual and verbal/physical abuse frequency does not add additional risk for COD to those who already have one disorder.

Being born in the United States significantly increases the COD hazard for those with one disorder by 59.6% compared to those who are born elsewhere (SE = 0.116, $p<0.001$). Both Blacks and Asian Americans have a lower hazard of COD than Whites, but there is no difference between Hispanics and Whites. Being male increases COD risk. Age is negatively associated with COD hazard.

The familial history variables are associated with increases in the hazard ratios for COD. Having COD in either one's biological mother or father is associated with a 38.4% increase in the hazard ratio of COD. Psychiatric disorder only in a parent increases the hazard ratio by 19.3% and SUD only by 25.6%. Family configuration, not knowing your parent's disorder status, and family support growing up are not significantly associated with COD hazard for those who already have a disorder, net of other factors.

The new variable for disorder sequence contributes some interesting findings to the model. Having psychiatric disorder first compared to having SUD first was associated with the largest hazard ratio in Model 6.2, with an HR of 1.361 (SE =0.071, $p<0.001$), or an 36.1% increase in risk of subsequently developing COD, as displayed in Table 6.4. This signals the importance of accounting for disorder sequence when seeking to understand onset of COD.

6.5 Hazard of Co-occurrence Given One Disorder by Gender

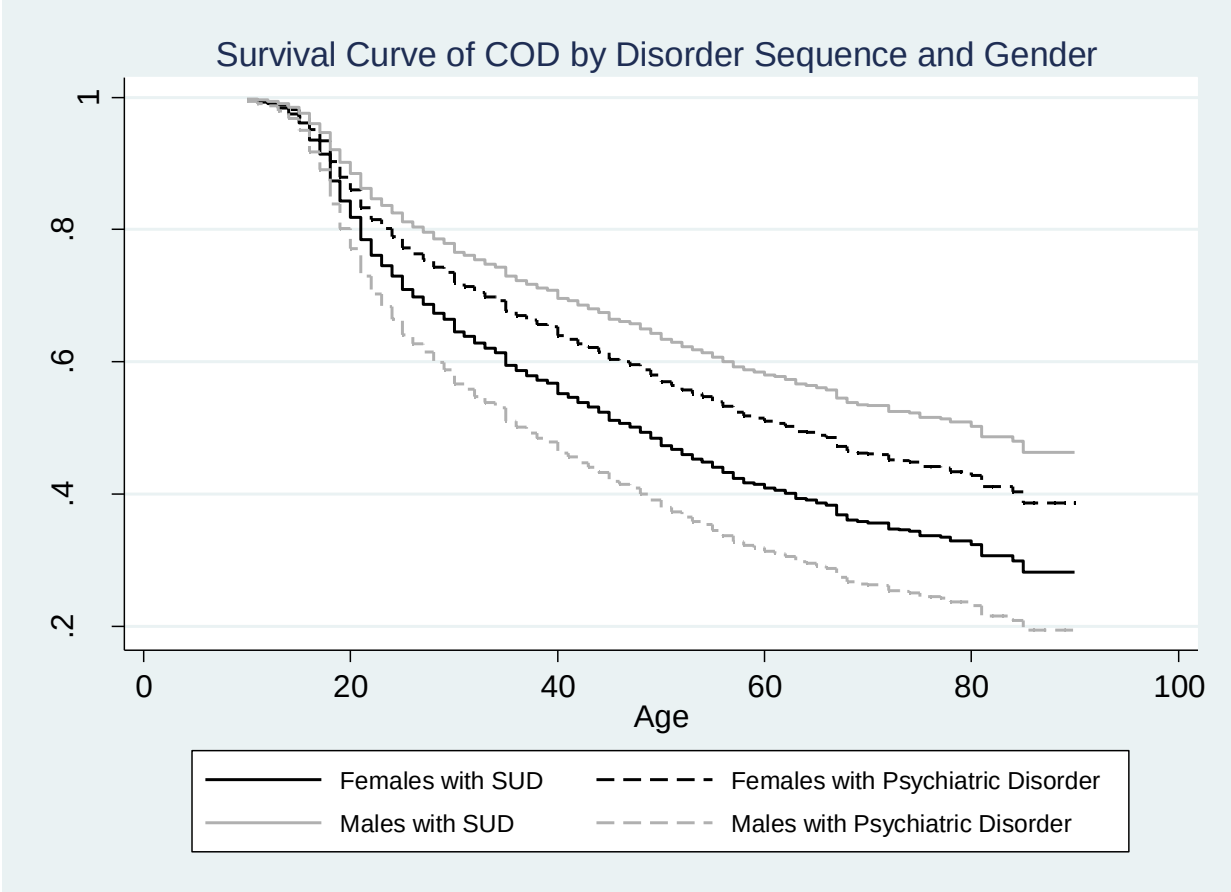
Based on the literature, I expect COD to develop differently for males and females –an expectation I repeatedly test in this dissertation– and this may also be partially related to the order in which males and females develop disorders. I test this possibility because I suspect that developing the "gender atypical" disorder of SUD for females may carry even more severe social and psychological consequences than the development of a "gender typical" psychiatric disorder, and that these consequences may lead to increased likelihood of developing COD. To test if the sequence of disorders matters differently for males and females (Hypothesis 3f), the product interaction term disorder sequence × male is introduced into a model with all of the covariates from Model 6.2, which becomes Model 6.6.

Table 6.4 on page 186 shows Model 6.2 and Model 6.6, which is the Cox Proportional Hazard model that interacts the effect of gender with disorder sequence and finds a significant conditional effect. The product interaction term for disorder sequence and gender is significant (HR = 2.832, SE = 0.222, $p<0.001$), and as such I reject the null hypothesis (H0: $\beta_{\text{disorder sequence} \times \text{gender}} = 0$ or $HR_{\text{disorder sequence} \times \text{gender}} = 1$) that the rate of co-occurrence for those with substance use disorder (compared to psychiatric disorder) is the same for males and females. The conditional relationship of sequence of disorder and gender is discussed below in detail. Table 6.4 shows two Cox Proportional Hazard Models, both with the sample of people who have experienced any disorder: one is the main effects model (Model 6.2) and the other the conditional model (Model 6.6).

The difference in the effect of having a psychiatric disorder for males relative to females is given by the co-efficient for psychiatric disorder × male, which indicates that males with psychiatric disorder have a 183.2% greater hazard ratio for COD compared to their female peers.

The coefficient for ‘male’ in the model gives effect of being male (relative to female) on COD given SUD, indicating a lower hazard (HR = 0.609, SE = 0.042, p<0.001). The effect of having psychiatric disorder for females (relative to SUD) is associated with a hazard ratio of 0.752 (SE = 0.044, p<0.001). The calculated effect of having psychiatric disorder for males (0.752 × 2.832) is associated with a hazard of COD that is 113.1% higher (HR = 2.131, SE = 0.146, p <0.001) relative to SUD for males. These trends are most easily seen in Figure 6.3 below which shows four survival curves with the impact of disorder sequence on COD by gender.

Figure 6.3 Survival Curve for COD Given One Disorder by Disorder Sequence and Gender



Overall, hazard of co-occurrence for males is higher than females in the event they psychiatric disorder, but not SUD. The hazard of co-occurrence for females (both who

experience SUD and who experience psychiatric disorder) is higher than males with a substance use problem, but lower than males who have psychiatric disorder.

6.6 Hazard of Co-occurrence Given One Disorder by Race/Ethnicity

Shifting from an investigation of the differential effects by gender to look at race/ethnicity, it is also possible COD develops differently for different racial/ethnic groups based on sequence of disorder once they already have one disorder. The theory reviewed in the *Background Literature* section for this dissertation suggest that SUD may be more socially sanctioned for Hispanics and Asian Americans than for Whites. If this is the case, it is possible that Hispanics and Asian Americans who develop SUD first are socially ostracized and face additional social and psychological burden that leads to COD. To test whether or not the order of disorders matters differently for racial/ethnic groups in the sample, as hypothesized in Hypothesis 3f, I test a model with the interaction term race/ethnicity × psychiatric disorder and find it to be non-significant using an Adjusted Wald test (F statistic (9,105)= 1.37, p =0.255), indicating it is reasonable to assume the effects of disorder sequence on COD do not differ by race/ethnicity.

6.7 Hazard of Co-occurrence Given a Psychiatric Disorder

Following the results above showing dramatic gender differences based on disorder sequence, I stratify the analysis to restrict the model first to look at COD hazard just those who had a psychiatric disorder. I stratify the analysis by disorder sequence for ease of interpretation of the interactions, as planned and described in section *3.9.7 Hypothesis Testing for Relationships in Survival Analyses*. By doing this stratification, I am deliberately separating the sample to describe the hazard for people who have a psychiatric disorder, and people who have

SUD distinctly, and I am allowing all parameters to vary freely for those two groups, meaning that it will not be possible to compare the effects of covariates between these two groups. This is an important theoretical decision that I make based on my assessment that the process of COD development is occurring differently depending on which type of disorder one develops.

The stratified analysis for risk of COD given a psychiatric disorder is shown in Model 6.4 Table 6.5, below. The survival and hazard function curves for the analysis in Model 6.4 can be seen in Figure 6.4 below. The hazard for developing COD given that one already has a psychiatric disorder is greatest between ages 20-30, it peaks at age 25 and declines over the life course after that. Two periods of more dramatic drops in risk are observable: between ages 30-40 there is a reduction in the hazard function and after age 60 there is another steep decline. Risk seems to be steady between ages 40-60.

Figure 6.4. Survival Curve and Hazard Function for COD, Given a Psychiatric Disorder (n=10,020)

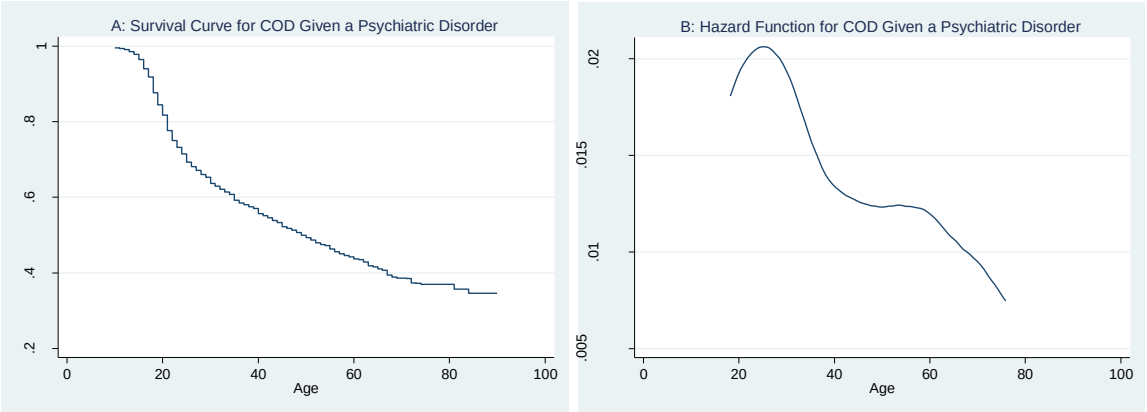


Table 6.5. Cox Proportional Hazard Model of COD Hazard Given a Psychiatric Disorder

	Model 6.4 Sample with a Psychiatric Disorder (n=10,020)		
Characteristic	HR		S.E.
Age (years)	0.956	***	0.002
Male (/female)	1.697	***	0.070
Race (/NH White)			
NH Black	0.728	***	0.041
NH Asian	0.680	**	0.086
Hispanic	0.869	ǂ	0.047
US-Born (/foreign born)	1.654	***	0.127
Childhood family structure (/two biological parents)			
Reconstituted families	1.004		0.055
Single parent	0.923		0.056
Other	0.982		0.125
Family support (/no)	1.063		0.049
Family history variables			
Family history COD (/no COD)	1.321	***	0.057
Family history unknown (/known)	0.967		0.128
Family history SUD (/no SUD)	1.326	***	0.085
Family history psychiatric disorder (/no psych disorder)	0.984		0.036
Childhood Poverty (/no)	1.030		0.058
Childhood Adversity Variables			
Childhood Adversities (Count)	1.028	**	0.008
Early Sexual Abuse (Freq)	1.017		0.033
Early Verbal and Physical Abuse (Freq)	1.026		0.032

Note: SE = robust standard error, HR = hazard ratio

ǂ p<.05; ** p<.01; *** p<.001, Analytic significance level is set to p=0.01 to account for multiple comparisons

For those who have a psychiatric disorder, age is negatively associated with COD hazard. Being Black or Asian American were both associated with lower risk compared to being White. Being male increased the likelihood of COD for those with a psychiatric disorder by 69.7% (HR= 1.697, SE = 0.070, p<0.001). Having COD and SUD only in the family history were both associated with an increase hazard ratio of developing SUD after already developing a

psychiatric disorder (for COD history HR= 1.321, SE = 0.057, p<0.001; for SUD history HR= 1.326, SE = 0.085, p<0.001). Having a family disorder with psychiatric disorder only did not increase COD hazard for those who have a psychiatric disorder.

Childhood adversities are positively associated with COD for those who have a psychiatric disorder, adding only a small additional hazard of 1.028 (SE = 0.008, p = 0.004) for every adversity experienced. This analysis showed no significant association between childhood poverty and COD for those who have a psychiatric disorder, leading me to reject Hypothesis 3c, that risk of co-occurrence for those who have a psychiatric disorder will be greater for those who experienced childhood poverty than those who did not.

6.8 Hazard of Co-occurrence Given a Substance Use Disorder

I then restrict the analysis to those who had SUD to look at COD in this group. This analysis is shown in Model 6.5, Table 6.6, below. The survival and hazard function curves for these analyses can be seen in Figure 6.5 below as well. The hazard of COD for those with SUD is greatest in the early 20's and the risk for those who have not yet developed a second disorder after they are 30 years is relatively lower than the risk before age 30. This hazard drops further after age 40 and declines steadily until age 60. Visually, the hazard seems to increase after age 60 again, but may not be a statistically meaningful difference as it is likely due to a small proportion of people with SUD interviewed after age 60, a phenomenon known to affect the appearance of hazard functions (Cleves, 2008).

Figure 6.5 Survival Curve and Hazard Function for COD, Given a Substance Use Disorder (n=4,445)

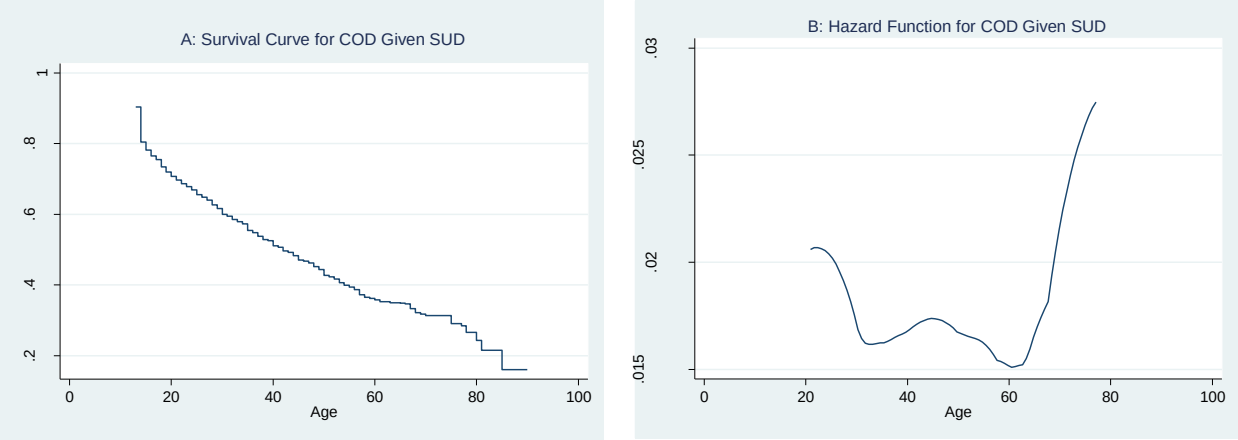


Table 6.6. Cox Proportional Hazard Model of COD Hazard, Given SUD

	Model 6.5 Sample with SUD (n=4,445)		
Characteristic	HR		S.E.
Age (years)	0.963		0.003
Male (/female)	0.609	***	0.046
Race (/NH White)			
NH Black	0.905		0.108
NH Asian	0.616	ǂ	0.144
Hispanic	1.073		0.124
US-Born (/foreign born)	1.202		0.209
Childhood family structure (/two biological parents)			
Reconstituted families	0.884		0.080
Single parent	1.074		0.117
Other	1.039		0.229
Family support (/no)	1.048		0.095
Family history variables			
Family history COD (/no COD)	1.500		0.115
Family history unknown (/known)	1.073	***	0.108
Family history SUD (/no SUD)	1.353		0.261
Family history psychiatric disorder (/no psych disorder)	1.983	***	0.156
Childhood Poverty (/no)	1.011		0.100
Childhood Adversity Variables			
Childhood Adversities (Count)	1.019		0.016
Early Sexual Abuse (Freq)	1.099		0.105
Early Verbal and Physical Abuse (Freq)	1.140		0.080

Note: SE = robust standard error, HR = hazard ratio

ǂ p<.05; ** p<.01; *** p<.001, Analytic significance level is set to p=0.01 to account for multiple comparisons

For risk of developing a psychiatric disorder after already having SUD (i.e., COD), having psychiatric disorder in one of the biological parents added an increased hazard of 98.3% (SE = 0.156, p <0.001) for COD likelihood, and not knowing the family history increased the hazard as well. Being male was associated with a 60.9% decrease in COD hazard, compared to being female (SE = 0.046, p <0.001). No other variables were significant in the model. This

stratified analysis restricted to those who had SUD with no psychiatric disorder preceding it showed no significant association between any of the variables of childhood adversity and COD.

6.9 Chapter Summary

Chapter 6 added important elements of time and sequence to the analysis of COD risk in accordance with the life course principles in the conceptual model for this dissertation. I showed that age of onset for disorders differs for those with COD from those who do not have COD, and also differs based on disorder sequence (within the group that develops COD). These univariate and bivariate trends are also seen in the Cox Proportional Hazard Models. This Chapter showed a clear gender difference in the impact of sequence of disorder, where have an SUD is more hazardous for women in terms of their likelihood of developing COD and psychiatric disorder is more hazardous for men in terms of their likelihood of developing COD. This analysis supports looking at risk factors associated with COD for those who have SUD distinctly from risk factors for those who have psychiatric disorders.

CHAPTER 7: DISCUSSION

In this chapter, I start by summarizing the key findings from this dissertation as they relate to each Aim. I comment on trends within the findings as well as inconsistencies between some of the results. Then, the limitations inherent in this study are presented along with an estimation of the impact they have on the findings from this dissertation. I list the major advances that are brought to the field of COD research with this research, and the strengths of the study. Finally, I discuss the public health implications and the future directions of COD research that are implicated based on the findings.

7.1 Discussion of Major Findings

7.1.1 Childhood Adversity Findings and Implications

A significant proportion of people experience stressors before age 18. These findings are consistent with other literature reporting high levels of childhood adversity (Evans et al., 2017) in the population. I found that having at least one adversity is more common for males than females. There were racial/ethnic differences in adverse experiences as well as gender differences as was found in previous waves of NESARC data by Evans and colleagues (2017). Whites tend to have higher levels of certain types of adversity than Blacks and Hispanics, and Asian Americans fair the best with low levels of all types of adversity.

Childhood adversity, both in terms of number of stressful experiences and also in terms of frequency of two particular experiences, childhood sexual abuse and physical/verbal abuse, is associated with higher relative risk ratios for COD. Generally, this relationship exists whether the association is assessed for people who have COD relative to SUD only, psychiatric disorder

only, or no disorder, although there are variations in which types of adversities are impactful depending on the comparison outcome. This finding is consistent with the strong relationship between childhood adversity and increased risk for occurrence of substance use and psychiatric disorders seen in the literature (e.g., Dube et al., 2002; Afifi et al., 2012; Green et al., 2010; McLaughlin et al., 2012).

The childhood adversity operationalization analyses done for this dissertation indicated that the summative score is helpful because it remains an important predictor of COD across all of the models analyzed here. This finding confirms reports in the literature (Shilling et al., 2009). However, I show that it is especially important to incorporate sexual abuse frequency and also frequency of physical and verbal abuse, which may differentiate clusters of adversities that occur together in the population, on top of number of childhood adversities. Others have indicated the importance of isolating types of adversity in their work (Turner, Finkelhor, & Ormrod, 2006; Turner & Lloyd, 2003) but this has not resulted in the adoption of different ways of operationalizing adversity. This dissertation adds a new perspective to the field regarding the best way to measure and use adversity in the study of COD.

The importance of both count and frequency measures is an important finding: it supports existing knowledge about the severe detrimental impact of childhood adversities on psychiatric outcomes, but it adds additional insight by showing that adverse experiences are associated with COD regardless of whether the risk is assessed relative to psychiatric disorder only or SUD only. COD, then, is an outcome that is highly associated with stressful early experiences, and this suggests differential social risk profiles that separate those who develop COD from those who have psychiatric disorders or alcohol/drug disorders alone.

7.1.2 Aim 1 Findings and Implications: Total Sample

I make several important discoveries concerning the relationship between poverty before age 18 and COD. I discover that on a bivariate level, childhood poverty is directly associated with COD, however, with the addition of childhood adversities and other covariates, there is no longer a direct association between poverty and COD. This suggests, only inferentially, that the relationship between poverty and disorder outcomes is operating indirectly or is spurious. If it is indirect, and poverty is actually only harmful because it is the vehicle to other negative experiences that determine disorder outcomes, it is an interesting finding. This implies that even in the absence of being able to increase income in the childhood home, there could still be amelioration of negative outcomes by intervening in the social experiences that are proliferated by poverty: including possibly delaying age at first substance use. Other possibilities include ameliorating negative effects of poverty through the development of other resources that were not measured in this study (such as psychological skills of coping, self-esteem, and mastery).

There are clear race/ethnicity differences in prevalence of disorder when COD is studied in the population as a whole. For COD relative to no disorder, Blacks, Asian Americans, and Hispanics, are all approximately half as likely as Whites to have COD, net of other factors, however, the relationship between poverty and COD does not vary by race/ethnicity. Nor does relationship between adversity and COD vary by race/ethnicity. Given this, I conclude that the early social determinants of co-occurring psychiatric disorder and SUD do not operate differently for those belonging to the White, Black, Asian American and Hispanic race/ethnicity groups.

There are, however, gender differences in both the likelihood of disorder outcomes (no disorder, SUD only, psychiatric disorder only, and COD) and the associations between childhood

poverty and COD as well as childhood adversity and COD. This work supports further investigation of the impact of status characteristics on COD, through their propensity to affect exposure to stressors— an approach that is underscored by the sociological study of stress (Pearlin, 1989) theoretical framing that I take in this dissertation. I show here that the impact of these childhood experiences on disorder can best be understood for males and females separately because it is likely that the development of disorder happens in distinct ways for males and females.

7.1.3 Aim 1 Findings and Implications: Males

For males, demographic factors remain important to the development of COD. Most of the race/ethnicity differences in COD are between COD and no disorder, with all other racial ethnic groups being less likely to have COD than White males. This is an interesting discovery: race/ethnicity is not as significantly associated with COD when it is compared to psychiatric disorder or SUD only. There are almost no racial/ethnic differences between males with one type of disorder and those with two types. US born males have substantially higher relative risk of COD than those born abroad.

Another interesting finding for males comes from the family functioning variables: family history of any type differentiates COD from no disorder, but for COD and psychiatric disorder only it is only family history of SUD that matters. Similarly, in comparing COD to SUD only, family history of psychiatric disorder significantly differentiates the two outcomes. These associations make sense, given that if there is a genetic component operating in disorder risk, for example, SUD in the family would be expected to increase the risk of the outcomes that involve substance use (COD and SUD), and thus to make the development of COD more likely than psychiatric disorder or no disorder, but not to make the development of COD any more likely

than SUD. With SUD in the family history it could also be that learning unhealthy coping mechanisms from the parent, socialization, and availability of substances makes the development of COD more likely than psychiatric disorder only.

Age of first substance use for males is associated with COD across all comparison outcomes. Scholars point to the vulnerability of the brain before age 21 and note that using harmful substances early in life may causes changes in the brain that create susceptibility to disorder (Heim et al., 2010). Earlier age of first substance use may also be capturing some of the negative effects of having a peer group that promotes risky behavior and may thus indicate additional social risk for future disorder.

Finally, it is very apparent that the social and material environments that males grow up in are associated with COD. In some cases, like with early poverty, it is a differentiating factor just between two outcomes. Childhood poverty distinguishes whether males have SUD or COD, with exposure to economic adversity in childhood being associated with higher relative risk of COD, net of other factors. In other cases, as with early adversities, the relative risk pervades all disorder comparisons made between COD and other outcomes. The count of childhood adversities that males are exposed to before age 18 is associated with COD relative to all other outcome categories. Sexual abuse frequency is associated with COD relative to SUD and no disorder, only. Physical/verbal abuse frequency is associated with increased COD likelihood relative to SUD and no disorder only.

7.1.4 Aim 1 Findings and Implications: Females

Now, I bring attention to some of the factors that impact lifetime occurrence of COD for females. Demographics are important for females in their associations COD risk. Black females have lower relative risk ratios of COD compared to all other outcomes than White females,

meaning they are more likely to have no disorder and one disorder than two disorder types than their White counterparts. This is a strong protective race effect that holds across all the categories of disorder compared. Asian American females are indistinguishable from White females in disorder outcomes: this is an important finding that may have been obscured in previous research that typically shows a mental health advantage for Asian Americans (Breslau et al., 2005). Perhaps by considering males and females together, the mental health advantage of Asian American males is decreasing the prevalence rates overall and giving the appearance that these benefits extend to females as well, which they do not in this analysis.

Many familial factors are significantly associated with COD, for females. The presence of family support is associated with a higher relative risk of COD, net of all other factors, but only when compared to no disorder. This is a paradoxical finding: one would expect family support to confer an advantage and protect from some of the harmful effects of childhood stressors on disorder outcomes. Perhaps feeling as though people believe in you and support you is an additional stressor if you are a female with a psychiatric disorder and SUD, and causes stress due to fear of disappointing loved ones. It may also be the case that a supportive family is indicative of being surrounded by others who are highly functional and successful, creating a chasm between those with a disorder and those without, and increasing stress that leads to COD. At the bivariate level family support is significant in the opposite direction for females, indicating that this kind of support is associated with lower relative risk of COD, as would be expected, and indicating the presence of suppression. Further research is required to ascertain the effect of family support on COD for females in the population.

For females, family history of any type differentiates COD from no disorder, and the same associations exist here as the ones seen for the males. Only history of SUD matters in

comparing COD to psychiatric disorder, and all family history except the biological mother or father's SUD matters when comparing COD to SUD.

For females, as was also the case when the analysis was restricted to males, age of first substance use is associated with COD (except when compared to SUD). These repeated findings stress the importance of delaying age of first substance use for as long as possible in adolescence as a preventative strategy for COD.

Childhood poverty distinguishes females who have SUD from females who have COD, with exposure to economic adversity in childhood being associated with lower relative risk of COD, a counter intuitive finding. The count of childhood adversities that females are exposed to before age 18 is associated with COD relative to psychiatric disorder and no disorder. Sexual abuse frequency and physical/verbal abuse frequency are associated with COD relative to SUD and no disorder, only. Thus, for females, the number of adversities is associated with increased COD likelihood relative to psychiatric disorder, but for COD relative to SUD it is more the frequency of abuse experiences that matters. Overall, the experiences that one has before the age of 18 are clearly associated with COD for females and represent an important period to intervene in for the development of disorders.

7.1.5 Aim 2 Findings and Implications

Aim 2 tested conditional relationships between childhood adversities and childhood poverty, and whether or not any such conditional relationship is operating differently by gender and by race/ethnicity. I rejected all of the hypotheses related to the conditional relationship between childhood adversities and childhood poverty. It is surprising that there is no moderation of the childhood poverty and COD relationship by number of adversities, given the inter-relatedness of economic and social adversity and the tendency for stressors to proliferate and

have non-linear relationships with each other (Anderson et al., 2002). However, this study confirmed that there is no conditional relationship between childhood poverty and childhood adversities when looking at COD, and this is still the case even when accounting for the possibility of differences in this relationship by race/ethnicity and gender. In concert with the results from Aim 1, this suggests that it is status characteristics, particularly gender, rather than the specific stressors used in this study that change the relationship between poverty and COD, again, supporting a sociological study of stress approach to understanding COD. To further understand the childhood adversity and poverty relationship for COD, mediation analyses would be a logical next step if this becomes mathematically possible in the future. Alternatively, operationalizing COD differently may allow the use of this measurement approach to test mediation of childhood poverty by adversity for COD.

7.1.6 Aim 3 Findings and Implications

This study contributes original findings to the understanding of when COD onsets, and it does so using recent data that are representative of the US population. On average, those with COD who have SUD first typically have their disorder onset in the early 20's and then have their psychiatric disorder onset in their early 30's on average. For those with COD who develop psychiatric disorder first (this is the majority of those with COD), onset happens much earlier, in adolescence, on average, and the development of SUD occurs in the mid-twenties.

At the population level, prior to the presentation of this dissertation research, it was not clear what distinguished COD risk from the risk of developing a single disorder type. This research shows that there are distinctive risk factors that can set individuals on a track to developing COD itself.

Upon restricting the survival analysis to those who have at least one disorder, these trends indicate that the count of adversities continues to distinguish people with COD from those with one disorder also and that these factors carry substantial risk, not just for the development of any psychiatric disorder or SUD alone, but specifically for the development of *both* of these.

Amongst those with at least one disorder, having psychiatric disorder compared to having SUD is associated with a 36.1% increase in hazard of subsequently developing COD. It turns out that not only does sequence of disorder matter for the development of COD, but it matters contrarily for males and females. The significant conditional relationship between disorder sequence and gender shows that risk of co-occurrence for males is higher than females in the event that they experience psychiatric disorder, but not SUD. The risk of co-occurrence for females (both who experience SUD and who experience psychiatric disorder) is higher than males with a substance use problem, but lower than males who have psychiatric disorder.

To understand the gendered nature of disorder outcomes seen in this dissertation, I draw on some of the life course literature related to timing, developmental stages, gender, and psychiatric outcomes. Because adolescent girls are typically more invested in the relationships they develop with parents, siblings, friends and romantic partners than adolescent boys (Leadbeater et al., 1999, Rudolph 2002), females are accordingly more likely to experience stress when these relationships are disrupted, and internalize these emotions, sometimes leading to disorder (most typically, a mood or anxiety disorder). If the development of the first disorder for females is SUD, this may create even more social dissonance than the presence of a different type of disorder. As female substance use is more socially sanctioned than male substance use (Keyes et al., 2011) and females have much lower rates of SUD than males overall, having SUD for females is a relatively uncommon experience. The social problems experienced as a result of

the SUD developed, then, for females, may increase the likelihood of experiencing a subsequent psychiatric disorder.

The tendency for females to be more likely than males to have COD after they have SUD may be due to the added stress associated with the development of SUD as described above, something I refer to as stress associated with a "gender atypical" disorder for females. Similarly, for males, if they develop a mood or anxiety disorder, for example (disorders which are much less common for males), they may be more likely to develop COD due to stress faced by the burden of a gender atypical first disorder. Males with SUD are the least likely to go on to develop COD. It is possible that this is due to the social support present for males with addictions, or possibly because of the tendency for these disorders to get resolved over time even in the absence of intervention.

The findings in this dissertation show, additionally, that for females with psychiatric disorder, they are less likely to go on to develop COD over the life course than males with a psychiatric disorder. It could be that females tend to have a later onset of their first disorder (Rudolph & Hammen, 1999), and thus have already passed through the period of highest risk for SUD by the time they develop a first psychiatric disorder, or that they do not face as much additional stress after the development of a psychiatric disorder because this is not an atypical disorder for females.

Regardless of the mechanisms driving these gendered differences, this dissertation research asserts findings that were previously unknown about disorder sequence for males and females, and the risk of COD after the development of a psychiatric disorder or SUD.

7.2 Limitations of the Study

This dataset has some perplexing findings regarding gender differences in some of the sample characteristics that were presented. Females reported higher levels of family history of disorder than males. It is possible that this is due to females being more likely than males to know their psychiatric family history due to stronger social and familial bonds, or perhaps that females are more comfortable disclosing this history than males, or it could indicate selection or selective recall issues. Similarly, females and males had different rates of childhood poverty and statistically significant differences in family configuration while growing up. This could, as above, be due to gender differences in the awareness of the social and material environment growing up, or it could indicate systematic bias being selected into the study, most likely based on self-selection. It is expected that these characteristics would be balanced by gender in the population, and the fact that they are not is an indication that there may be selection issues, selective recall issues, or reporting differences that are impacting the findings presented here.

This study draws clear lines between childhood poverty, childhood adversity, parental disorder, and the subsequent development of disorders in individuals. However, in reality, these constructs are not as easily divided as I have represented them. For example, childhood disorders are a source of stress for the whole family, and these affect the stress levels in the whole home environment possibly influencing parental disorder or exposure to other adversities. Depending on how early the disorders onset, the direction of causality may be reversed: it may in fact be children who affect their parents and the familial environment. It is unlikely that this is the case, given the mean age of onset for most disorders and strict inclusion of only independent variables that occurred before age 18, but it is still possible. If this is the case, and the direction of causality is reversed, the inferential errors made are that instead of childhood adversity affecting

COD, it could be that COD actually affects childhood adversity and poverty, or that the events are non-linear in their occurrence. This research, therefore, is aided by the other studies that exist, with longitudinal data, that have been able to distinguish the separate and distinct influences of poverty, and adversity, on psychiatric disorder, and that these occur in the temporal manner hypothesized in the dissertation (Varese et al., 2012).

Another important limitation of this research is that the dataset is cross-sectional, rather than longitudinal. Longitudinal analysis, while allowing for more confidence in the causality of the associations tested, is not possible presently with the available data. The measures used enable only retrospective assessment of childhood poverty, adversities and disorder, as well as several other important contextual variables. Retrospective cross-sectional data carry inherent weaknesses: most critically that they are more subject to recall bias and do not allow for causality to be ascertained as strongly as prospective methods do. For the findings in this study, it means that I cannot be certain that the associations are operating in the directions I expect or that the associations are indicative of true causal relationships.

This study is limited by the retrospective recall of age of onset used in the survival analysis. Ideally, to enhance the strength of the survival analysis, this type of analysis would be conducted with longitudinal data. Similarly, it is ideal if the unit of analysis for the survival models is more precise than age in years, the unit of measurement used. Age in years can lead to ties in survival time, which should happen in only rare circumstances, under optimal situations. It is unlikely that these issues significantly impacted the trends seen in this dissertation, but more precision would be desirable to discern the hazard of COD over time. For this limitation, it is likely that onsets of disorders that happen more recently, or temporally close to the time of interview would be remembered with more accuracy, potentially biasing the results to be less

accurate for disorders that develop earlier in the life course.

Regarding the potential for recall bias, associations with adverse events and psychiatric disorder were also observed in studies which employed other, more rigorous, methods to assess trauma exposure (Varese et al., 2012), and it is therefore likely that the associations presented here are valid. There is evidence that the retrospective self-assessment of childhood trauma tends to underestimate rather than overreport the occurrence of trauma (Hardt & Rutter, 2004) and studies have demonstrated the validity and reliability of retrospective reports of trauma, showing that they are stable across time, relatively unaffected by current symptoms, and report are generally concordant with other sources of information (Varese et al., 2012).

Measurement limitations include the limited measures of childhood poverty available in NESARC-III. By using receipt of government assistance before age 18 as a measure of poverty, people who are not eligible for these kinds of benefits but who are still living in poverty, especially immigrants, may be misclassified as not being exposed to childhood poverty. This lack of information on childhood poverty, and the likely misclassification of some people who grew up in poor households as having no exposure to childhood poverty may result in the estimates for the association between childhood poverty and COD being underestimated. Having more information on socioeconomic position in the households in which respondents grew up would be ideal, as well as more information on the ameliorative resources available during childhood such as: friend support networks, religious support and personal coping characteristics during childhood like self-esteem and mastery. More information on ameliorative resources during childhood would allow for a more complete test of the stress process model and would provide information about whether these resources help to mitigate the effects of adversity on

COD. This information would help to tell a more fulsome story, and is something, hopefully, that can be addressed in postdoctoral research using other datasets.

7.3 Strengths of the Study

There are several strengths of this study that make it exemplary in the field of COD research. The use of population data to study the phenomenon of COD is something done rarely in the existing literature, but as shown in this dissertation, it can be very instructive in identifying trends and association at the population level that are not possible to establish in clinical datasets. This dissertation uses a large, nationally representative, recent dataset designed specifically to collect information on substance use and psychiatric disorder making it ideally suited for the study of epidemiological phenomena. I consider multiple psychiatric disorders and SUD together, to show patterns than exist in COD development generally, without restricting the sample to disorder- or substance-specific outcomes. Because of the strength of the dataset and the innovative questions asked in this study, I provide analysis of current trends and establish associations that exist in the population, make a substantial contribution to COD research.

Testing for conditional relationships is critically lacking in existing COD literature and as a result there is a risk of misunderstanding the relationship between childhood experiences and resulting substance use and psychiatric disorder. Indeed: I show here that assuming childhood experiences are the same for males and females obscures the true relationships. For example, for males childhood poverty increases relative risk of COD compared to SUD and for females childhood poverty decreases relative risk. Not testing for the conditional relationship, as most other studies do, prevents the true nature of the relationship from being discovered. The dissertation research presented here does not repeat the mistaken assumptions about conditional

relationships and provides an analysis that is able to detect the presence of conditional processes in COD development.

Through proper specification and analysis of childhood stressors, this study allows for detailed understandings of the most influential types of stressors for different groups in developing COD, and it answers questions about thresholds and the nature of the relationship between different stressors with the outcome of COD.

One notable strength of this study is the precision in measurement that is applied to the dependent variable. Separating COD from SUD, psychiatric disorder, and no disorder in one study is rare in the literature, but allows for a precision in estimation of the effects attributable to COD as distinct from just one type of disorder or no disorder. A frequent shortcoming of the current research is the muddling of multiple groups in the comparison, where people with COD are only compared to those with psychiatric disorder, which only tells a partial story. Furthermore, most research about psychiatric disorders is conducted completely separately from research about SUD, despite the relatedness of the two disorder types and the common comorbidity. This dissertation helps to bridge the divide between research in the two related fields of mental health and addiction that typically research outcomes in silos.

This study controls for some of the genetic influence on disorder by including variables related to the biological mother and father's disorders. Including variables for parental disorder may be a conservative estimation of the biological risk added for an individual because it also likely includes unmeasured shared environmental influences such as neighborhood characteristics. Nonetheless, I show above and beyond these familial risk factors that childhood experiences are important variables that are strongly associated with COD development.

The use of the Cox Proportional Hazard Model takes into consideration that some

observations are “censored” and reduces censorship bias, adding a strong methodological contribution to the literature in this field. Finally, using a large, recently collected, nationally-representative survey dataset with sample weights allows the conclusions to be generalized to the US population and increases the external validity of the findings: a clear strength of this study.

7.4 Innovative Contributions of the Study

This work advances the field of COD research in several ways, providing answers to many of the current uncertainties in the literature, including the following: what relationship exists between childhood poverty and COD for males and females, and the differential impact of childhood adversities on COD for males and females; as well as how disorder sequence affects risk of COD by gender.

In addition, I apply key innovations to the dissertation research that move this field of inquiry forward. Consistent with my inclusion of the Life Course Perspective, I use a time-dependent measure of COD (age of onset) to investigate how stressors influence timing of COD: something completely missing from current COD research. This study looks at age of onset across disorders all together in the population, something rarely done in the published literature, using recent data, and thus, this information represents meaningful new knowledge for the field, that advances the understanding of life course development of COD. This example of how I integrate theory with my investigation of social factors that are associated with COD is something that is an important departure from the norm with COD research. The bulk of studies conducted on co-occurring substance use and psychiatric disorder are undertaken in the absence of theoretical underpinnings to guide the work.

Testing different operationalizations of childhood adversities allows this study to be responsive to the suggestion that stressors may accumulate and influence each other in a more

complicated manner than simply as an additive sum. The testing of multiple interactions investigates the way that poverty, gender, and race/ethnicity may together produce different outcomes– rather than independently. Further investigation is needed to determine how and why childhood adversity functions as an important early source of stress related to the occurrence of COD in adulthood, and something that can now be built upon the foundation I set with this study. For example, it may be that childhood adversity precipitates a series of stressors, a process known as stress proliferation (Pearlin, 1985; Pearlin et al., 2005), where as an individual progresses through the life course, they accrue more stressors and suffer more adverse events, collectively creating circumstances that build stress and diminish capacities to avoid adverse mental health outcomes. The stress accumulation and resource mitigation beyond childhood was not measured in this study and would be an instructive future direction for analyses.

My focus on social factors associated with development of COD rather than biological or genetic risk is something I contribute to the body of knowledge on COD. Many studies highlight the genetic components of disorder development, and by instead turning the focus to the childhood social and material environment, I bring the spotlight to factors that are modifiable.

In summary, this research advances the scientific literature on COD by providing information on the connections between poverty and stressors in childhood and their linkage to COD for males and females. This is the first study to my knowledge to present research on race/ethnicity and gender differences in the early social factors that affect COD with sufficient sample size to properly test associations. Further, the survival analysis used in this dissertation shows the timing of disorder onset and how disorder sequence matters differently by gender: an assumption previously untested in this body of work.

7.5 Public Health Implications

The significant burden of COD for people with psychiatric disorders and on national healthcare expenditures is clear. COD is a public health concern because it represents serious and largely unaddressed health issues for a substantial proportion of the population. This study's focus on childhood poverty, childhood stressors, and COD considers some of the earliest and most socially determined antecedents of later psychiatric and SUD.

This research has clear public health relevance: above and beyond the genetic risk incurred by having a parent with a disorder, experiencing adverse events in childhood is associated with COD, whether it is compared with a single type of disorder or no disorder. Thus, efforts to help children and adolescents develop strategies to cope with adversity are important and may be able to curb a significant amount of added risk due to harmful early experiences.

Mental health outcomes in particular are often thought of as being genetically determined, and while genetics are important to consider, the social determinants of psychiatric disorder represent areas of risk that are modifiable and occur in segments of the population in such a way that designing interventions to ameliorate these risks is possible.

These race/ethnicity and gender findings have implications for programming and a systematic approach to prevention. It is clearly important to develop prevention programs that differ for males and females, based on the results of this work, including programs that take into account sequence of disorder. Specifically, targeting females who develop SUD in the absence of a psychiatric disorder may be a beneficial strategy: these women are at increased risk of COD, relative to their peers, and early intervention for this group could improve outcomes. The same is true for males who develop a psychiatric disorder, they may benefit from early intervention to prevent SUD from developing.

Finally, studying the nature of poverty and adversity demonstrates and investigates the unfair chains of disadvantage that aggregate non-randomly in society. Paying attention to the systematic and avoidable differences in fundamental causes of poor health outcomes is an essential part of public health (Link & Phelan, 1995), and makes this research especially relevant to public health.

7.6 Conclusions

This study showed that despite a bivariate relationship between childhood poverty and COD, with the addition of childhood adversities and other covariates, there is no longer an association between poverty and COD. Childhood adversities, however, tend to be strongly associated with COD, net of other factors.

There are clear gender differences operating in the development of COD. Gender differences are seen in both disorder prevalence and the associations between childhood poverty and COD as well as childhood adversity and COD. Childhood poverty is associated with COD in opposite directions for males and females: for males it increases the relative risk ratio of COD compared to SUD, and for females it decreases the relative risk for this same comparison.

The significant conditional relationship between disorder sequence and gender found shows that risk of co-occurrence for males is higher when they experience psychiatric disorder (relative to SUD). On the contrary, the risk of co-occurrence for females is higher when they have SUD. In the absence of accounting for this, as most past research has not, a blanket assumption about risk of co-occurrence being higher with a particular disorder type is made for the whole population.

This study helps to bridge the gap between research on psychiatric disorder and SUD by assessing the prevalence of co-occurrence in relation to the presence of only one disorder, by analyzing how childhood factors make this co-occurrence more or less likely, and by showing temporal trends in the development of COD for those with an existing psychiatric disorder distinctly from those with existing SUD: all information which is currently missing at the population level.

This research has clear public health implications: controlling for all other factors, experiencing adverse events in childhood is associated with COD. Since COD is common, and patients that develop both substance use and psychiatric disorder incur high treatment costs and account for a larger proportion of national health care expenditure than those with only one disorder, prevention efforts in this area are essential. Thus, efforts to help children and adolescents develop strategies to cope with adversity are important and may be able to curb a significant amount of added risk due to harmful early experiences, as well as reduce significant public health expenditures.

Appendices

APPENDIX A. Model Building and Assessment of Proportionality for Model 6.1

	Model 6.1			
Variable	x^2 value Shoenfeld's test (df)		x^2 value Log Rank test (df)	
Age (years)	92.94 (1)	***	N/A	
Male (/female)	0.82 (1)		37.18 (1)	***
Race (/NH White)			338.71 (3)	***
NH Black	21.61 (1)	***		
NH Asian	0.01 (1)			
Hispanic	12.49 (1)	***		
US-Born (/foreign born)	1.84 (1)		516.80 (1)	***
Childhood family structure (/two biological parents)			716.09 (3)	***
Reconstituted families	0.03 (1)			
Single parent	2.05 (1)			
Other	0.14 (1)			
Family support (/no)	0.60 (1)		119.92 (1)	***
Family history variables				
Family history COD (/no COD)	0.30 (1)		2769.66 (1)	***
Family history unknown (/known)	0.36 (1)		84.79 (1)	***
Family history SUD (/no SUD)	2.42 (1)		54.10 (1)	***
Family history psychiatric disorder (/no psych disorder)	2.88 (1)		881.16 (1)	***
Childhood Poverty (/no)	0.10 (1)		766.57 (1)	***
Childhood Adversity Variables				
Childhood Adversities (Count)	5.35 (1)	*	N/A	
Early Sexual Abuse (Freq)	1.35 (1)		N/A	
Early Verbal and Physical Abuse (Freq)	1.83 (1)		N/A	
Psychiatric Disorder (/SUD)	N/A		N/A	

APPENDIX B. Cox Proportional Hazard Model of Lifetime COD Risk with Time-Varying Coefficients

	Model 6.1 With time-varying coefficients		
Characteristic	HR		SE
Age (years)^	0.941	***	0.002
Male (/female)	1.337	***	0.039
Race (/NH White)			
NH Black	0.470	***	0.028
NH Asian	0.572	***	0.083
Hispanic	0.608	***	0.036
US-Born (/foreign born)	2.594	***	0.162
Childhood family structure (/two biological parents)			
Reconstituted families	0.968		0.036
Single parent	1.008		0.039
Other	1.166		0.102
Family support (/no)	1.105	*	0.038
Family history variables			
Family history COD (/no COD)	1.912	***	0.066
Family history unknown (/known)	1.273	**	0.106
Family history SUD (/no SUD)	1.441	***	0.054
Family history psychiatric disorder (/no psych disorder)	1.793	***	0.054
Childhood Poverty (/no)	1.066		0.037
Childhood Adversity Variables^			
Childhood Adversities (Count)	1.101	***	0.007
Early Sexual Abuse (Freq)	1.104	**	0.024
Early Verbal and Physical Abuse (Freq)	1.127	***	0.025

Note: SE = robust standard error, HR = hazard ratio

ǂ p<.05; ** p<.01; *** p<.001, Analytic significance level is set to p=0.01 to account for multiple comparisons

^time-varying effect of variable accounted for with time-varying coefficient method

APPENDIX C. Model Building and Assessment of Proportionality for Model 6.2

	Model 6.2			
Variable	x^2 value Shoenfeld's test (df)		x^2 value Log Rank test (df)	
Age (years)	100.29 (1)	***	N/A	
Male (/female)	5.04 (1)	*	53.85 (1)	***
Race (/NH White)			41.28 (3)	***
NH Black	21.94 (1)	***		
NH Asian	0.06 (1)			
Hispanic	11.02 (1)	***		
US-Born (/foreign born)	1.60 (1)		78.52 (1)	***
Childhood family structure (/two biological parents)			132.87 (3)	***
Reconstituted families	0.25 (1)			
Single parent	2.34 (1)			
Other	0.61 (1)			
Family support (/no)	0.84 (1)		3.05 (1)	
Family history variables				
Family history COD (/no COD)	0.08 (1)		392.07 (1)	***
Family history unknown (/known)	1.56 (1)		39.32 (1)	***
Family history SUD (/no SUD)	0.01 (1)		19.49 (1)	***
Family history psychiatric disorder (/no psych disorder)	5.80 (1)	*	29.26 (1)	***
Childhood Poverty (/no)	0.08 (1)		134.74 (1)	***
Childhood Adversity Variables				
Childhood Adversities (Count)	0.58 (1)		N/A	
Early Sexual Abuse (Freq)	0.08 (1)		N/A	
Early Verbal and Physical Abuse (Freq)	0.02 (1)		N/A	
Psychiatric Disorder (/SUD)	86.24 (1)	***	30.02 (1)	***

APPENDIX D. Cox Proportional Hazard Models of COD Hazard Given One Disorder with Time-Varying Coefficients

	Model 6.2 With time-varying coefficients		
Characteristic	HR		SE
Age (years) ^	0.982	***	0.002
Male (/female)	1.439	***	0.062
Race (/NH White) ^			
NH Black	0.654	***	0.039
NH Asian	0.707	*	0.102
Hispanic	0.777	*	0.047
US-Born (/foreign born)	1.737	***	0.106
Childhood family structure (/two biological parents)			
Reconstituted families	0.960		0.036
Single parent	0.977		0.038
Other	0.962		0.085
Family support (/no)	1.061		0.036
Family history variables			
Family history COD (/no COD)	1.405	***	0.048
Family history unknown (/known)	1.103		0.093
Family history SUD (/no SUD)	1.276	***	0.048
Family history psychiatric disorder (/no psych disorder)	1.191	***	0.036
Childhood Poverty (/no)	1.007		0.035
Childhood Adversity Variables			
Childhood Adversities (Count)	1.037	***	0.006
Early Sexual Abuse (Freq)	0.982		0.022
Early Verbal and Physical Abuse (Freq)	1.009		0.022
Psychiatric Disorder (/SUD)	1.836	***	0.101

Note: SE = robust standard error, HR = hazard ratio

ǂ p<.05; ** p<.01; *** p<.001, Analytic significance level is set to p=0.01 to account for multiple comparisons

^time-varying effect of variable accounted for with time-varying coefficient method

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