

ABSTRACT

Title of Dissertation: THE RELATIONSHIP OF EARLY SOCIAL, MENTAL,
AND BEHAVIORAL EXPERIENCES WITH ADULT
OBESITY AND ALCOHOL USE DISORDER

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Stressful life events early in life, including symptoms of mental disorders or childhood maltreatment, may increase risk for worse mental and physical health outcomes in adulthood. The purpose of this dissertation was to examine the effects of childhood Attention Deficit Hyperactivity Disorder (ADHD) symptoms and maltreatment experience on two adult outcomes: obesity and alcohol use disorder (AUD). Mediation effects of adolescent characteristics were explored. This dissertation used Waves I, III, and IV of the National Longitudinal Study of Adolescent to Adult Health.

In Paper 1 (Chapter 3), we investigated the association between multiple types of child maltreatment and adult objective (body mass index; BMI) and subjective (self-rated) obesity, as well as mediating effects by adolescent characteristics including depressive symptoms and BMI. Results showed that after adjusting for sex, race/ethnicity, and maternal education, physical maltreatment was moderately associated

with adulthood obesity as measured by BMI and self-reported obesity, while sexual maltreatment was more strongly associated with the objective measure but not the subjective measure. The indirect effects of mediation of adolescent BMI and depressive symptoms were statistically significant.

In Paper 2 (Chapter 4), the objective was to examine mediation by adolescent depressive symptoms, alcohol consumption, peer alcohol consumption, and delinquency in the relationship between ADHD symptoms and adult AUD. The indirect effects of mediation of adolescent delinquency, alcohol consumption, and peer alcohol consumption were statistically significant in single and multiple mediator models.

In Paper 3 (Chapter 5), the objective was to assess the joint effects of maltreatment/neglect on adult AUD. After adjusting for sex, race/ethnicity, child maltreatment, and parental AUD, ADHD symptoms were significantly associated with increased odds of AUD. There was no strong evidence of multiplicative interaction by maltreatment. This association was stronger for males than females, although the interaction term was not statistically significant.

This dissertation adds to the literature by examining relationships between several major public health problems: ADHD symptoms, childhood maltreatment, AUD, depressive symptoms, and obesity. This project has implications for understanding how early life stress increases risk for later physical and mental health problems, and identifying potential intervention targets for adolescents.

THE RELATIONSHIP OF EARLY SOCIAL, MENTAL, AND BEHAVIORAL
EXPERIENCES WITH ADULT OBESITY AND ALCOHOL USE DISORDER

by

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Chapter 1: Introduction

1.1. Background and rationale

It is well recognized that stressful life events can have a negative impact on one's physical and mental health. A stressful life event may induce anxiety, depression, change in diet, or changes in other behaviors that immediately impact health. For example, consider the stereotypes of the previously healthy widower who passes away shortly after his wife does, the child who is diagnosed with depression after losing a parent, or the recent divorcée who gains weight due to stress. However, the impact of stress is not limited to the short term; stress can also affect health in the long term as well.

Researchers and clinicians have noted that individuals with alcohol use disorder (AUD) are more likely to report past traumatic or stressful events, such as physical or sexual maltreatment during childhood (e.g., Dube et al., 2002; Enoch, 2011), although sometimes with mixed results. Childhood maltreatment has also been associated with markers of physical health in adulthood such as obesity (Midei & Matthews, 2011), possibly due to some of the same adolescent mediational mechanisms such as depressive symptoms. Similarly, ADHD symptoms in childhood, which can cause stress on the child's self-image, social relationships, school experience, and relationships with parents, may be associated with greater risk of AUD in adulthood (Charach et al., 2011).

However, few studies have explored in depth what factors may be confounding or mediating these associations, even though it is likely that there are multiple possible mediational variables reflecting adolescent behavior and health on the causal pathway between child experiences and adult health. Adulthood obesity and alcohol use disorder may both arise from the development of inappropriate coping mechanisms in childhood

and/or adolescence, as a direct consequence of stressful events experienced in childhood. For example, when faced with stress or negative feelings, the individual turns to behaviors such as binge eating or binge drinking in order to self-medicate and feel better. However, there is not enough research on these longitudinal relationships between experience, behavior, and health.

More research on some of the risk factors and causal pathways between childhood stressful events and adult health outcomes is needed, to better understand the mechanisms of these associations, and to identify targets for early intervention for adolescents who may be starting to follow a dangerous path that leads to poor adult health outcomes. The National Longitudinal Study of Adolescent to Adult Health (Add Health) provides an ideal dataset to study these relationships, due to the fact that the data set is large, nationally representative, and longitudinal. **In this dissertation, the relationships between childhood stressful experiences (ADHD symptoms and maltreatment or neglect), adolescent characteristics and behaviors (depressive symptoms, delinquency, alcohol consumption, and body mass index), and adulthood health (obesity and AUD) will be explored, with the purpose of highlighting two key messages: 1) the importance of considering an individual's social and mental history as potential risk factors for a diagnosis of obesity or AUD, and 2) warning signs in adolescence that call out for early intervention, to reduce the risk of poor health outcomes in adulthood.**

1.1.1. Literature Review: Chapter 3 (Paper 1).

Childhood Maltreatment. Childhood maltreatment refers to any act by a parent or caregiver that results in potential harm, actual harm or threat of harm to a child

(intentional or unintentional). Maltreatment may refer to physical abuse, sexual abuse, emotional abuse, or neglect. According to data collected from the National Child Abuse and Neglect Data System (NCANDS), in the year 2009, there were about 702,000 unique cases of child maltreatment in the U.S., with a rate of about 9.3 victims per 1,000 American children (U. S. Department of Health and Human Services, 2010). Because these rates are dependent on reporting to authorities, many cases may go undetected, and therefore these rates are likely underestimated. Statistics based on self-report in national and community surveys are more inclusive and generally report much higher incidence rates (Gilbert et al., 2009); one study based on the National Longitudinal Study of Adolescent to Adult Health reported that 28.4% of respondents reported at least one occurrence of physical abuse, 4.5% of respondents reported at least one occurrence of sexual abuse, and 41.5% of respondents reported at least one occurrence of supervision neglect (Hussey et al., 2006). Fang et al (2012) used secondary data from sources such as Child Protective Services to estimate that each nonfatal case of child maltreatment results in an average lifetime cost to society of \$210,012, including health care, adult medical costs, productivity losses, child welfare costs, criminal justice costs, and special education costs (Fang et al., 2012). Given these high incidence estimates and lifetime costs, child maltreatment is far too common, too costly, and a serious health concern for the United States.

Child maltreatment has both short term and long term effects on an individual's physical and mental well-being, as well as on their pattern of health behaviors (Gilbert et al., 2009). For example, maltreatment is a risk factor for lower educational achievement and socioeconomic well-being in adulthood (Currie & Widom, 2010; Zielinski, 2009),

mental health problems (Edwards et al., 2003), adolescent violence (Duke et al., 2010; Fang & Corso, 2007), and adolescent delinquency (Ford et al., 2010). Early trauma such as maltreatment can alter brain development, i.e., altering the stress response systems of the brain, resulting in increased long term risk for conditions such as Post-Traumatic Stress Disorder (PTSD), depression, Attention Deficit Hyperactivity Disorder (ADHD), and substance abuse (Teicher et al., 2002). These consequences of child maltreatment can have a social and economic impact on a population, including increased costs of healthcare and government services such as child welfare (World Health Organization, 2016).

Certain family and child characteristics can increase a child's risk of being mistreated. Younger age of child, being unwanted, or having special needs can increase one's general risk (World Health Organization, 2016). Sex is also associated with type and severity of maltreatment; males are generally at slightly higher risk for physical abuse, especially major acts of physical abuse and serious injury, while females are at higher risk for sexual abuse (Barnett et al., 2005). Parental AUD has also been shown to increase an individual's risk of being maltreated, although studies have shown inconsistent results (Widom & Hiller-Sturmhofel, 2001).

Obesity. According to the CDC, more than a third of American adults today are obese, representing a drastic increase since 1990. Obesity is associated with chronic health conditions such as sleep apnea and osteoarthritis; it can also reduce life expectancy due to increased risk of serious health conditions such as heart disease, stroke, diabetes and certain types of cancer. Obesity is related to increased medical costs; the CDC estimates that in 2008, medical costs related to obesity could have risen to \$147 billion,

or almost 10% of all medical spending in the U.S. (Centers for Disease Control, 2013). Thus, obesity is a dangerous and costly condition that is highly prevalent in American society today. When treating a patient with obesity, it is important to consider the whole patient, including potential risk factors of obesity, such as stressful or traumatic childhood experiences.

It is not only adults who are affected by the growing rates of obesity in the U.S.; adolescents are also gaining weight as the American lifestyle includes more sedentary time and processed foods, and less physical activity. Thus individuals who are at greater risk for obesity may already show a propensity for overeating and higher body mass index in adolescence, and generally obesity is maintained into adulthood. A meta-analysis of over 200,000 participants from 15 cohort studies reported that 80% of obese adolescents were still obese in adulthood (Simmonds, et al., 2016). In addition, adolescents and young adults who are obese may already be experiencing physical morbidities such as diabetes and hypertension which will continue and worsen through adulthood (Cheng, et al., 2016). Therefore, it is important to consider obesity not just as an adult outcome at one point in time, but as a trajectory throughout adolescence and adulthood.

Maltreatment and obesity. Previous literature has shown that childhood maltreatment may be associated with later obesity. For example, Dube (2010) analyzed data from the Behavioral Risk Factor Surveillance System (BRFSS), from 5,378 adults living in Texas, and found that those who experienced childhood abuse and household dysfunction were 1.3 times more likely to be obese in adulthood than those who did not (Dube et al., 2010). A meta-analysis of 36 studies showed that childhood interpersonal

violence, including physical abuse, sexual abuse, and peer bullying, was positively associated with risk for obesity and central adiposity (Midei & Matthews, 2011). Furthermore, child maltreatment has been associated with health conditions such as Type 2 Diabetes due to higher body mass index (Rich-Edwards, et al., 2010).

Maltreatment's association with later obesity has been shown with different demographic groups. For example, data from the Black Women's Health Study showed that women who were exposed to child/teenager physical and sexual abuse were 1.29 times more likely (95% CI: 1.20-1.38) to have a body mass index (BMI) over 30; this relative risk decreased to 1.14 (95% CI: 1.08-1.21) after controlling for reproductive history, diet, physical activity, depressive symptoms, and SES (Boynton-Jarrett et al., 2012). In one study using Add Health data, the association between sexual and physical abuse and severe obesity ($BMI \geq 40 \text{ kg/m}^2$) was reported to be stronger for non-minority females than others (Hazard ratio=2.5, 95% CI: 1.3-4.8), although confidence intervals were large due to sample size (Richardson, Dietz, & Gordon-Larsen, 2014). In addition, the association between child maltreatment and obesity may be apparent as early as adolescence. In a retrospective study of 1,434 youths admitted to an inpatient psychiatric facility, a reported history of sexual abuse was associated with BMI above the 85th percentile (odds ratio=1.41); however, physical abuse was not associated with BMI (Keeshin et al., 2013). However, more research needs to be done to further explore the moderating effects of demographic variables such as sex and race/ethnicity.

One study, by Shin & Miller, used the Add Health dataset to study the association between child maltreatment and obesity. Using latent curve modeling, they showed that childhood neglect was associated with a faster average rate of BMI growth over time

compared to children who were not neglected ($p < .01$). Sexual abuse was also associated with faster rate of BMI growth ($p < .05$). The authors controlled for sex, race/ethnicity, SES, breastfeeding, depression in adolescence, relationship with parents, and parental obesity. They concluded that maltreatment was positively associated with BMI trajectories into adulthood, possibly due to elevating daily stress, using food as a coping mechanism, or by the promotion of unhealthy behaviors as a consequence of limited supervision (Shin & Miller, 2012).

The Role of Adolescent Depressive Symptoms. Depressive symptoms are sometimes controlled for as a confounding variable in studies of maltreatment and obesity, but not treated as a mediating variable (Danese & Tan, 2014). However, it is evident that childhood maltreatment is moderately associated with adolescent depressive symptoms (Hussey, Chang, & Kotch, 2006), which are then in turn associated with risk factors for obesity such as poor diet and lack of physical exercise (Hoare, et al., 2014). Individuals who are mistreated or neglected in childhood are more likely to struggle with increased stress levels, low self-esteem, and feelings of self-worthlessness, which can lead to developing inappropriate coping mechanisms, such as overindulging in food. Adjusting for depressive symptoms as a confounder has been shown to decrease the effect estimate between maltreatment and obesity, using a pooled estimate from six studies (Danese & Tan, 2014), which supports the possibility of indirect mediation; however, adjustment is not appropriate because depressive symptoms are likely on the causal pathway. Therefore, adolescent depressive symptoms are an often overlooked but logical mediator on the pathway between childhood maltreatment and adulthood obesity.

1.1.2. Literature Review: Chapters 4-5 (Papers 2-3).

Alcohol Abuse and Dependence. Drinking an alcoholic beverage is known to have a depressant effect on the central nervous system, and many people choose to drink alcohol for its pleasurable, relaxing effect. In the 2013 National Survey on Drug Use and Health, slightly more than half of Americans reported being current drinkers of alcohol (Substance Abuse and Mental Health Services Administration, 2013). Moderate use of alcohol is common and not problematic in most cases. However some individuals will use alcohol in a maladaptive pattern by drinking to excess, developing cravings, and drinking alcohol despite incurring consequences such as legal, social, and health problems. Symptoms such as these are present in individuals with an alcohol use disorder (AUD), which may include alcohol abuse, or abuse with dependence. Alcohol abuse and dependence are considered psychiatric disorders and therefore defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). DSM-IV criteria for alcohol abuse includes recurrent alcohol use impairing performance at work, home or school, recurrent alcohol use in situations in which it is physically hazardous (e.g. driving, etc.), recurrent alcohol-related legal problems, and continued use despite social or interpersonal problems due to alcohol use (e.g. fighting with one's spouse). To be diagnosed with alcohol abuse, the individual must not meet criteria for dependence, which implies more physical symptoms and more severe consequences. DSM-IV criteria for alcohol dependence include increasing tolerance to alcohol, withdrawal symptoms after stopping use, using more alcohol than intended, unsuccessful attempts to quit, spending a lot of time obtaining, using, and recovering from alcohol, giving up activities because of

alcohol use, and continued use after knowledge of recurrent physical or psychological sequelae (American Psychiatric Association, 2000).

The use and abuse of alcohol represents a large public health burden for the United States. According to the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) in 2001-2002, 8.5% of adults over 18 had experienced an alcohol use disorder in the past year (4.7% abuse, 3.8% dependence), and 30.3% had experienced an alcohol use disorder in their lifetime (17.8% abuse, 12.5% dependence) (Hasin et al., 2007). Alcohol use, abuse, and dependence cause preventable health problems such as cirrhosis of the liver, and contribute to early mortality rates. Alcohol is reported to be the third leading cause of death in the U.S., after tobacco and poor diet/physical inactivity (Mokdad et al., 2004). Alcohol is a major factor in traffic fatalities due to impaired motor function and attention; according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA), 39.5% of traffic crash fatalities in 2004 in the U.S. were alcohol-related (Yi et al., 2006). Alcohol use is a costly problem for the American workforce, increasing healthcare expenditures as well as contributing to employees' missed work days. People inebriated with alcohol may make poor choices and engage in violence or risky behaviors such as unprotected sex, putting them at risk for sexually transmitted infections such as HIV. Although there are now many counseling and treatment options for alcohol use disorder, treatment is expensive and time consuming, with unsatisfactory efficacy rates (Ferri et al., 2006). Thus research that focuses on precursors and risk factors of AUD will be beneficial to recognizing red flags and opportunities for intervention in adolescence, before the individual develops a more serious problem resulting in health consequences in adulthood.

Attention Deficit Hyperactivity Disorder. Children with Attention Deficit Hyperactivity Disorder (ADHD) display symptoms of attentional difficulties and/or hyperactivity/impulsivity, which leads to trouble staying focused on one activity for an extended period of time. These symptoms affect performance at school, at home, and possibly later, at the workplace; symptoms persist into adulthood for many patients. The prevalence of ADHD has increased in recent years, at least in part due to increasing rates of diagnosis and fewer cases going undiagnosed. According to the National Center for Health Statistics, about nine percent of American children have a diagnosis of ADHD; this represents an increase from about seven percent in 1998-2000 (Akinbami et al., 2011).

The etiology of ADHD remains somewhat unclear, although genetic factors likely play a role (Khan & Faraone, 2006). According to DSM-IV criteria, there are three types of ADHD: predominantly inattentive type, predominantly hyperactive-impulsive type, and combined type. Inattentive symptoms include not listening or paying attention, not following through on instructions or tasks, having trouble organizing activities, avoiding tasks that take a lot of mental effort over a long period of time, often losing things needed for tasks or activities, and being easily distracted or forgetful. Symptoms of hyperactivity or impulsiveness include fidgeting, not sitting still, excessive and inappropriate running/climbing, feelings of restlessness, trouble doing activities quietly, excessive talking, blurting out answers or interrupting, and having trouble waiting one's turn. A child must have symptoms present before the age of 7 years old, and must have clinically significant impairment in social, school, or work functioning in order to be diagnosed with ADHD (American Psychiatric Association, 2000).

Depressive symptoms. Depression is a mental health condition characterized by low/depressed mood, anhedonia (inability to enjoy activities previously found to be enjoyable), and sometimes low energy, for a period of time lasting more than two weeks (American Psychiatric Association, 2000). Depression is fairly common; according to a report from the CDC, about 1 in 10 Americans report depression (Centers for Disease Control, 2012). Depression affects all aspects of a person's life, from relationships with family and friends, to productivity at work, and can have health consequences as extreme as suicide in some cases. Depression is also associated with increased risk of chronic disease such as cardiovascular disease; for example, a recent meta-analysis reported that those with depression had an adjusted hazards ratio of 1.45 (95% CI: 1.29-1.63) for total stroke (Pan et al., 2011). This association between depression and disease may be partly due to increased stress, and lessened motivation to take care of oneself with diet, exercise, and seeking treatment for disease symptoms. Overall, depression is a serious and life-altering condition with many mental, social, and physical symptoms and consequences.

ADHD Symptoms and Depressive Symptoms. Children with ADHD display higher rates of comorbid mental health disorders such as depression; a recent meta-analysis of 29 cross-sectional and longitudinal studies found a moderate positive association between ADHD and depression among children and adolescents under 21 (Meinzer, Pettit, & Viswesvaran, 2014). Mental health constructs such as depression have been associated with experiencing past stressful events, which may include experiences associated with ADHD symptoms such as troubled relationships with teachers, parents, and peers (Fletcher, 2009). Experiencing a stressful event can lead to negative feelings,

lower self-esteem, and even suicidal ideation (Barnett et al., 2005). Early childhood adversity can disrupt the development of brain structure and function, and lead to maladaptive methods of coping with future stress and adversity (Shonkoff et al., 2012). The inability to use adaptive coping methods may cause negative feelings and depressive symptoms. In addition, an individual with ADHD symptoms may have depressive symptoms due to feelings of inadequacy or failure in the school or workplace. This “demoralization” theory of ADHD symptoms and consequences leading to depressive symptoms has received mixed support in the literature, and other authors have suggested additional possible explanations for the observed comorbidity, including shared etiology, shared genetic factors, and overlapping symptoms such as an emotion regulation deficit (Meinzer, Pettit, & Viswesvaran, 2014). Therefore, the relationship between ADHD and depression is complex and multilayered.

Depressive Symptoms and Alcohol Use Disorder. Mental health disorders such as clinical depression have been associated with alcohol abuse (Davis et al., 2008), as the individual may turn to abusing alcohol in order to dull their feelings or avoid coping with their feelings (Thornton et al., 2012). In fact, depression and alcohol abuse have a very high co-morbidity; meeting DSM-IV criteria for either alcohol use disorder or major depression carries a three to fourfold increased risk of meeting criteria for the other (Grant & Harford, 1995). A recent literature review reported that after adjusting for sociodemographic and other confounders, an association between depression and alcohol use disorder remains, with pooled adjusted odds ratios between 2.00 and 2.09 (Boden & Fergusson, 2011). In addition, alcohol acts as a depressant and sedative in the brain, possibly exacerbating depressive symptoms through neurophysiologic and metabolic

changes in the brain (Boden & Fergusson, 2011). Finally, alcohol dependence and depression may have similar risk factors, such as experiencing traumatic life events. Therefore depression and its symptoms are very closely tied to alcohol use disorder.

Delinquency. Adolescent delinquency refers to participation in illegal behavior by minors; this can include behaviors that are illegal for any citizen, such as vandalism or illegal drug use, as well as status offenses that are dependent on the person being a minor, such as truancy from school or underage smoking/drinking. Every year, there are about 5,804 arrests for every 100,000 individuals between ages 10-17 in the United States (Office of Juvenile Justice and Delinquency Prevention, 2012). Arrest rates are higher for males (7,885 per 100,000) than females (3,619 per 100,000); by race, arrest rates are highest for Blacks (11,157 per 100,000), then Whites (4,968 per 100,000), and then lowest for Asians (1,947 per 100,000) (Office of Juvenile Justice and Delinquency Prevention, 2012). These numbers only represent those who are arrested for delinquent behaviors; many more adolescents who perform delinquent behaviors go undetected. To a certain extent, some delinquent behavior may be somewhat normative for adolescents, as it is a time of increased rebellion, impulsivity, and exploration for many (Steinberg, 2008). Some delinquent behaviors are common for many American adolescents; almost half of 12th graders report using alcohol in the past 30 days (Windle, 2003). Other delinquent behaviors may be more serious, have worse consequences, or be repeated often enough that they become problematic. For example, some adolescents may get into physical altercations on occasion, but fewer adolescents will use a potentially lethal weapon such as a knife or gun. Individuals who demonstrate delinquent behavior in adolescence may be at increased risk of long term health outcomes including increased

mortality in adulthood as well; in a cohort study that followed delinquent and non-delinquent boys from Boston, the authors found that the men who were consistently delinquent in adolescence were twice as likely to die by age 65, mostly due to poor self-care in adulthood (such as infections or accidents) and alcohol abuse (Laub & Vaillant, 2000). It is clear that delinquency has important consequences for adolescents not only in the short term, such as getting in trouble in school and with parents, but also in the long term for health.

ADHD Symptoms and Delinquency. ADHD symptoms such as attentional difficulties and hyperactivity/impulsivity affect performance and behavior at school and at home (American Psychiatric Association, 2000), possibly causing the child to experience adverse events such as poor grades and negative attention from parents, teachers, and peers. A child with ADHD symptoms may have trouble making friends due to hyperactive behavior that is construed by others as socially inappropriate, and a decreased ability to follow social rules. Early childhood adversity such as troubled relationships with parents, teachers, and peers can disrupt the development of brain structure and function, and lead to maladaptive methods of coping with future stress and adversity, such as alcohol use (Dube et al., 2002; Shonkoff et al., 2012). By adolescence, associating with delinquent peers and performing delinquent behavior such as skipping school, performing acts of vandalism, and drinking alcohol may be observed. Qualitative research suggests that another reason that adolescents with ADHD may associate with peers who use alcohol or drugs, and begin to use alcohol or drugs themselves, is to obtain a sense of belongingness with peers (Nehlin et al, 2015). In addition, adolescents with ADHD symptoms may find school frustrating and even pointless, which decreases

motivation to behave well and avoid trouble. In summary, the literature supports the association between childhood ADHD symptoms and adolescent delinquent behavior.

Delinquency and Alcohol Use Disorder. Delinquency during adolescence is associated with adulthood alcohol use disorder as well as drug use (White & Gorman, 2000). One study used structural equation modeling and data from the National Longitudinal Survey of Youth to test the association between antisocial behaviors in adolescence (including shoplifting, stealing, property damage, fighting, use of force, use of marijuana and other drugs, and drug trafficking) and adult alcohol use disorder in 7,326 individuals. The authors found that person offenses, property offenses, and early illicit substance involvement were all significantly associated with later alcohol dependence and abuse; early onset of alcohol use (earlier than 15 years of age) was associated with abuse only ($p < .01$) (Harford & Muthen, 2000). Another study of twins showed that engaging in five problem behaviors (smoking, alcohol use, illicit drug use, police trouble, and sexual intercourse) were all significantly associated with alcohol use disorder at age 20; specifically, females were 3.6 times more likely (95% CI: 2.1-6.4) and males were 5.0 times more likely (95% CI: 3.2-7.8) to meet DSM-III criteria for AUD if they reported alcohol use in adolescence. Furthermore, trouble with police (excluding traffic violations) was associated with an odds ratio of 5.9 (95% CI: 2.5-13.8) for females and 2.7 (95% CI: 1.6-4.7) for males for later alcohol use disorder (McGue & Iacono, 2005).

The Role of Child Maltreatment and Neglect. Adverse or traumatic life events can increase the risk of later health behaviors and conditions such as alcohol and drug abuse in adulthood (Enoch, 2011; Hser et al., 2007). For example, alcohol abuse is very

common in patients with Post-Traumatic Stress Disorder (PTSD), as alcohol is a depressant that has a relaxing effect and counteracts the high arousal symptoms of PTSD (Jacobsen et al., 2001). Several studies have validated the association between childhood maltreatment (physical, emotional, sexual, or neglect) and increased risk of alcohol abuse in adulthood (Dube et al., 2002), including one longitudinal study that used propensity score matching to infer a causal relationship (Thornberry et al., 2010). Past maltreatment has also been associated with adolescent alcohol use and binge drinking (Hamburger et al., 2008; Kaufman et al., 2007; Shin et al., 2009). A previous study using data from the National Longitudinal Study of Adolescent Health (Add Health) showed an association between all types of maltreatment and adolescent alcohol use and binge drinking after controlling for age, sex, race/ethnicity, SES, immigrant generation, and region (Hussey et al., 2006); however, another showed that controlling for parental AUD rendered the association with physical abuse and alcohol use non-significant (Shin et al., 2009). Another study using a clinical sample of 9,346 HMO patients found that self-reported AUD in adulthood was 2.9 (95% CI: 2.3-3.6) times more likely in those who had reported emotional abuse during childhood, 1.9 (95% CI: 1.6-2.3) times more likely in those who reported physical abuse, and 1.9 (95% CI: 1.6-2.4) times more likely in those who reported sexual abuse (Anda et al., 2002). The relationship between child maltreatment and adult alcohol abuse has also been reported in international samples, such as in Taiwan (Yen et al., 2008) and New Zealand (Fergusson et al., 2008). In fact, the Taiwanese study reported that adolescents who had experienced childhood physical abuse were more than three times as likely to report problem drinking and depression in

adolescence (Yen et al., 2008). Thus there is a documented link between maltreatment during childhood and AUD in later life.

This relationship may be partly due to the individual using alcohol as a way to cope with or escape from trauma and related depressive symptoms, reduce feelings of isolation and loneliness, self-medicate in an attempt to gain control over the experience, and improve self-esteem (Widom & Hiller-Sturmhofel, 2001). In addition, an individual who has been abused may have mistrust of others, and a less close relationship with their parents, contributing to negative feelings. Using alcohol as a coping mechanism is a temporary and maladaptive strategy that does not solve the problem, so more and more alcohol is needed, eventually resulting in an alcohol use disorder in a significant number of maltreated individuals.

The Role of Sex of the Participant. Three of the variables under study, maltreatment, ADHD symptoms, and alcohol use disorder all have documented variations by sex. While childhood maltreatment in general is reported in equal rates for males and females (U. S. Department of Health and Human Services, 2010), rates may vary by type of maltreatment; males are at slightly higher risk for physical maltreatment, especially major acts of physical maltreatment, while females are at much higher risk for sexual maltreatment (Barnett et al., 2005). The prevalence of ADHD is well known to be higher for boys than girls (Akinbami et al., 2011). Sex affects rates of AUD; males are about twice as likely to suffer from alcohol abuse or dependence than females (SAMHSA Office of Applied Studies, 2004). Researchers have also found sex differences in self-reported reasons for using alcohol, rates of comorbidities such as depression and anxiety,

and treatment behaviors (Brady & Randall, 1999). For example women may be more likely to use alcohol to self-medicate mood disturbances (Brady & Randall, 1999).

Conclusions of Literature Review. From this literature review, we conclude that these social, mental, and physical health variables are all interrelated across multiple stages of life. Some variables are more obviously connected, and other relationships are less apparent and less well studied. More research regarding the mechanisms of how child experiences affect adult health would not only provide more knowledge and understanding, but also have important implications for possible warning signs and modifiable behaviors in adolescence, in order to prevent some poor health outcomes in adulthood.

1.2. Objectives/research questions

The overarching goal of this dissertation is to explore the relationship between stressful events in childhood and physical and mental health in adulthood, specifically the outcomes of obesity and alcohol use disorder, as well as explore possible effect modification, mediation, and confounding effects, using the nationally representative dataset of the National Longitudinal Study of Adolescent to Adult Health (Add Health). Specifically, the three specific aims and associated research questions are as follows:

Specific Aim 1 (Chapter 3). To assess the relationship between childhood maltreatment and obesity in adulthood.

a. Is childhood maltreatment associated with objective obesity as measured by body mass index in adulthood?

b. Is childhood maltreatment associated with subjective obesity as measured by a self-reported obesity variable in adulthood?

c. Effect modification: Are these relationships different for males and females?

d. Mediation by adolescent characteristics: Are there indirect effects of mediation of adolescent depressive symptoms in these relationships?

e. Mediation by adolescent characteristics: Are there indirect effects of mediation of adolescent body mass index in these relationships?

Specific Aim 2 (Chapter 4). To assess adolescent characteristics as potential mediators of the relationship between childhood ADHD symptoms and adult alcohol use disorder.

a. Mediation by adolescent characteristics: Are there indirect effects of mediation of adolescent depressive symptoms in this relationship?

b. Mediation by adolescent characteristics: Are there indirect effects of mediation of adolescent delinquency in this relationship?

c. Mediation by adolescent characteristics: Are there indirect effects of mediation of adolescent alcohol consumption in this relationship?

d. Mediation by adolescent characteristics: Are there indirect effects of mediation of adolescent peer alcohol consumption in this relationship?

Specific Aim 3 (Chapter 5). To examine childhood ADHD symptoms and maltreatment/neglect in relation to adult alcohol use disorder.

- a. Main association: Are childhood ADHD symptoms and childhood maltreatment/neglect in combination associated with adult alcohol use disorder?
- b. Effect modification: Is this relationship different for males and females?
- c. Effect modification: Is this relationship different for those whose parent has an alcohol use disorder?

1.3. Theoretical/conceptual framework and hypotheses

1.3.1. Specific Aim 1.

The Life Course Perspective describes the idea that events and environmental factors shape our personalities and behavior throughout the lifespan (Hser et al., 2007). Individuals who are mistreated in childhood are more likely to struggle with low self-esteem and feelings of self-worthlessness. This can lead to the individual developing inappropriate coping mechanisms, such as overindulging in food. Emotional eating, or “eating one’s feelings” can refer to eating food, especially “comfort food” that is high in fat and calories, in order to manage or satisfy negative emotions rather than to satisfy hunger. One may also stop taking care of oneself and engaging in healthy behaviors such as physical activity. Being obese can also lead to more feelings of low self-esteem and worthlessness, resulting in a vicious cycle. These patterns may begin in adolescence and continue into adulthood.

There is likely a physiological component to the association between childhood maltreatment and obesity. Researchers have shown that chronic stress is linked to

changes in cortisol levels and hypothalamic-pituitary-adrenal (HPA) axis activation, as well as the central sympathetic nervous system (Bjorntorp, 2001). The HPA axis is responsible for the body's reaction to stress, as well as regulating energy storage/expenditure and hormone production. Chronic stress can increase a person's allostatic load, which is a term that encompasses the physiological consequences of repeated or chronic stress over time (Berkman & Kawachi, 2000); an increased allostatic load is associated with negative health effects, both physical and psychological. HPA axis dysregulation and allostatic load are considered relevant in health outcomes such as heart disease, PTSD, ADHD, depression, and AUD (Berkman & Kawachi, 2000). Chronic stress brought on by repeated maltreatment or memories and lasting effects of maltreatment can therefore increase an individual's allostatic load, which affects stress behaviors (e.g. overeating or binge drinking), hormones that affect metabolism, and depressive symptoms, which are all linked with obesity. This has been shown in controlled animal studies; primates exposed to chronic stress over a period of two years are more prone to increased weight, increased fat, altered cortisol response, insulin resistance and coronary heart disease (Shively et al., 2009). Therefore a large part of the conceptual framework involves chronic stress, brought on by memories and lasting effects of maltreatment, causing alterations in physiology which are associated with obesity.

In addition, specific types of maltreatment may have different psychological effects on eating patterns. Sexual abuse victims may subconsciously try to make themselves unattractive to the opposite sex, which is possibly intended to prevent more sexual abuse. Individuals who experienced child neglect and didn't have enough to eat

growing up may overcompensate by overeating or hoarding food as an adult. A physically abused child who felt unloved or had an unstable living situation may turn to food as a steady source of comfort (Barnett et al., 2005). Therefore different subtypes of maltreatment may each have an effect on adulthood eating patterns and an individual's chances of obesity. Physical abuse, sexual abuse, and neglect are all associated with later self-esteem issues, social and emotional difficulties, and depression (Barnett et al., 2005). This is partly a result of the victim's negative thoughts, such as a perception that he/she deserves the abuse, or that the world is a bleak, punitive place. These negative thoughts may either be planted by the abuser or inferred by the victim. For example, a physical or emotional abuser may explicitly tell the victim that he/she is worthless, while a neglectful caregiver may indirectly express the notion that the child is not worth his/her time, and a sexual abuser may treat the victim as nothing but a sexual object with no other worth. The victim may then internalize these negative messages of self-worthlessness and turn to unhealthy coping mechanisms such as alcohol abuse to cope with both the negative thoughts and the resulting symptoms of depression. Feelings of self-worthlessness may also prevent from being motivated to avoid health consequences of abusing alcohol, if the individual doesn't believe that he/she deserves good health.

The work of Dr. Cathy Widom, a researcher who has studied the long term effects of child maltreatment for more than twenty years, also supports the hypothesized associations in Chapter 3 (Paper 1). Dr. Widom has published research which demonstrates how child maltreatment is associated with mental health in adulthood (Widom et al., 2007). She has also published research testing the theory of a "cycle of violence" in which childhood maltreatment is associated with later criminal and violent

behavior, as well as revictimization (Widom, 2012; Widom et al., 2006). Her body of work presents a strong case that childhood maltreatment causes many long term effects, including later depressive symptoms. This association may exist due to increased distrust of others, low self-esteem, and dysfunctional social relationships, that result from maltreatment.

Therefore, it is hypothesized that multiple types of childhood maltreatment and neglect are positively associated with adulthood obesity, as measured by both an objective and subjective measure, and that these relationships will be partially mediated by adolescent depressive symptoms. In addition, this pattern will already be apparent in adolescence, as proven by the indirect effect of mediation of adolescent BMI.

1.3.2. Specific Aim 2.

Dr. Aaron Beck, the father of cognitive therapy and the author of the Beck Depression Inventory, developed the Cognitive Theory of Depression (Beck et al., 1979), which states that depression is caused by negative thoughts about oneself, the world, and the future (the “Negative Cognitive Triad”). The depressed individual often has negative automatic thoughts, biases, and cognitive distortions, such as feelings of self-worthlessness. According to the theory, these negative thoughts then cause the negative mood and affect which are the symptoms of depression (rather than vice versa as other theorists had described). A child with ADHD symptoms may experience such negative thoughts about his or her abilities at school, social relationships, and place in the world, leading to depressive symptoms in adolescence. Thus, Beck’s Cognitive Theory of Depression provides part of the conceptual framework for this project, as it may explain

how stressful experiences during childhood result in negative thoughts about oneself and the world, leading to depressive symptoms and later alcohol use disorder.

Delinquency during adolescence, including alcohol consumption, may increase the risk of alcohol use disorder in adulthood for several reasons. Children diagnosed with ADHD may possibly seek out a calming agent such as alcohol to counteract the symptoms of ADHD, or use alcohol as a maladaptive coping mechanism to deal with stresses and negative experiences resulting from ADHD (Barkley, 2014). In addition, qualitative research suggests that individuals with ADHD may use alcohol/drugs to obtain a sense of belongingness with peers (Nehlin et al, 2015). Delinquent behavior may increase relationship problems between the adolescent and his/her parents, resulting in less parental social support for the individual. Performing the delinquent behavior may also contribute to the individual's lessening attachment to social norms and rules, and provide reinforcement for deviant behaviors which can include excessive alcohol use (White & Gorman, 2000). Additionally, during the delinquent act, the adolescent may form new associations with other deviant peers who are also engaging in other delinquent behaviors, and therefore the adolescent is introduced to these new behaviors (Fergusson et al., 2002). Thus the individual is more likely to commit more delinquent behaviors, which often include underage drinking. Earlier exposure to alcohol is associated with a higher risk of AUD (Merikangas & McClair, 2012), although it is controversial whether this association is causal. Thus an adolescent who engages in delinquent behavior including alcohol consumption may have higher risk of later AUD, for multiple reasons. In addition, association with peers and friends who engage in alcohol consumption

increases likelihood of adolescent alcohol consumption, on the causal pathway between ADHD symptoms and adulthood AUD.

In summary, it is hypothesized that the ADHD symptoms will have an effect on the individual's depressive symptoms and level of delinquency in adolescence, due to factors such as negative self-thoughts and decreased trust of others. In turn, adolescent delinquency may set an individual on a path of breaking rules and defying social norms, associating with deviant peers, lower achievement in school, and using illicit substances (including drinking alcohol while underage), which may result in a greater chance of alcohol use disorder in adulthood. Therefore, this paper tests the hypothesis that adolescent delinquency and depressive symptoms are potential mediating variables in the relationship between childhood ADHD symptoms and adulthood AUD.

1.3.3. Specific Aim 3.

The Life Course Perspective is a useful framework for studying alcohol use disorder, because of the dynamic nature of alcohol use/abuse behaviors and their risk factors (Hser et al., 2007); in other words, abusing alcohol is not an event that happens at one point in time, but it is a behavior that changes over time, and may be influenced by past and current life events. Early adversity and toxic stress contributes to adulthood disease, affecting the developing brain architecture as well as the coping/stress responses to future adversity (Shonkoff et al., 2012). Previous research has shown that experiencing adverse events such as childhood maltreatment or neglect is associated with later alcohol problems, and experiencing more of these events carries more risk than experiencing just one event (Dube et al., 2002). Similarly, a child with ADHD symptoms may experience negative stressful events such as getting into trouble at home and at school, getting poor

grades, or being bullied by peers due to their symptoms or behavior. These sources of stress may have cumulative effects on the individual's long term health outcomes.

In the first two papers, the negative effects of stress related to ADHD symptoms and childhood maltreatment or neglect are assessed with regards to adult health and health behaviors. The third paper builds on this work by assessing the joint effects of the two childhood exposures on adult AUD. Thus, this paper hypothesizes that alcohol use disorder is associated with childhood ADHD symptoms, as well as maltreatment or neglect, and individuals who experience both exposures may have greater odds of AUD in adulthood. Multiple variables were tested for potential confounding in the relationship between ADHD symptoms and adult alcohol use disorder. Interaction by child maltreatment and neglect was assessed in order to test the joint effects of maltreatment and ADHD. Parental AUD and sex were also tested for effect modification because of their relationships with both the exposure and the outcome variables as established in previous literature.

1.4. Innovation and significance

Alcohol use disorder and obesity are among some of the most pressing health issues in America today. They affect many millions of Americans and their families and have long lasting effects on both mental and physical health. Research that explores potential precursors and mechanisms of these poor health outcomes is crucial for increased understanding of which individuals may be more vulnerable, as well as methods of prevention and treatment.

1.4.1. Specific Aim 1.

Research that analyzes potential causes or risk factors of obesity is critical to recognizing at-risk individuals, and designing interventions for children, adolescents, and adults, to prevent and reduce the rate of obesity. Childhood maltreatment and neglect is one such risk factor that has been suggested to increase risk for adolescent and adult obesity, although this has not been definitively proven, and previous research on this topic has some limitations.

Some previous research has statistically controlled for sex, rather than testing sex for effect modification (Shin & Miller, 2012). We believe that it is important to also test sex as a potential effect modifier, because males and females are different in several key ways. First, males are more susceptible to different types of maltreatment (e.g. more physical abuse) than females (more sexual abuse). Second, females and males have different physiology as regards to metabolism and hormone levels which both affect body mass index. Third, females and males may have different risk of overeating as a method of coping with stress. Therefore, the present study will treat sex as an effect modifier. In addition, the longitudinal nature of the dataset allows the testing of the indirect effects of mediation by depressive symptoms in adolescence, using a validated scale of depressive symptoms, to test one pathway between childhood maltreatment and later obesity. Depressive symptoms are sometimes controlled for as a confounding variable, but few publications have tested its mediational effect. A relatively new and superior method of testing mediation effects is used. Extreme obesity ($\text{BMI} \geq 40 \text{ kg/m}^2$) in addition to the classic definition of obesity ($\text{BMI} \geq 30 \text{ kg/m}^2$) will be tested as an outcome, to test more severe obesity in light of the increasing prevalence of obesity in the U.S. Finally,

adolescent BMI will be also tested as a potential mediating variable, to test whether this maladaptive pattern begins in adolescence. It is beneficial to recognize and treat obesity in adolescence because it is harder to change long-established patterns, habits, and thought patterns in adulthood. In addition, many years living in a state of obesity has cumulative effects on the body such as joint pain (which makes exercise more difficult), and an adolescent still has time to prevent these future health consequences.

Another gap in knowledge addressed by this study is how differing types of maltreatment may be associated with adult obesity. Previous literature has been somewhat focused on sexual and physical maltreatment, possibly because these concepts are both easier to quantify and generally receive more media attention; this study will include those exposures as well as physical/supervisory neglect. Child neglect has been shown to have long term consequences on mental health, such as cognitive delays and emotional difficulties (Barnett et al., 2005). This project examines child neglect in relation with adult obesity. Therefore, this paper adds to the existing literature for this topic.

1.4.2. Specific Aim 2.

Traumatic life events have been shown to increase risk of depression, and depression is highly co-morbid with alcohol use disorder. ADHD symptoms are related to poorer school performance and social relationships, and associated with stress, negative thoughts, and depressive symptoms in childhood and adolescence, yet few other papers have examined the role of depressive symptoms as a potential mediator in the relationship between childhood ADHD symptoms and adult AUD. This paper addresses gaps in knowledge regarding whether the indirect effects of mediation of this variable

will be significant for the outcome of adult AUD, and whether the relationship differs by sex. A new and robust method of testing mediation is used.

Delinquency during adolescence is hypothesized to be directly associated with both childhood ADHD symptoms and adult AUD, and thus may appear on the causal pathway of the main association. However, adolescent delinquency has not been well studied as a potential mediator between childhood ADHD symptoms and later AUD, especially with a nationally representative cohort study such as Add Health. Multiple delinquent behaviors, including stealing, vandalism, and violence, as well as adolescent alcohol use, will be tested. These behaviors were self-reported, which allows greater sensitivity and subtlety than relying on court documented cases of delinquency. In addition, the mediating variable of adolescent friend alcohol consumption provides a unique way of measuring the hypothesis that individuals with ADHD symptoms seek out delinquent peers as friends, leading to more association with delinquent behaviors such as underage drinking.

This paper highlights that some adolescents who display depressive symptoms or delinquent behaviors may have another underlying mental health issue, such as ADHD symptoms that could be subclinical or undiagnosed, and these adolescents could be at greater risk for AUD later in life. Delinquent behavior and depressive symptoms are both often brushed off as being typical teen behavior, but this does a disservice to those who may really be struggling with stressful and negative feelings about themselves and their relationships with others. Therefore, it is important to recognize that some of these adolescents may benefit from diagnosis and/or treatment from a mental health professional.

1.4.3. Specific Aim 3.

The relationship between childhood ADHD symptoms and AUD in adulthood has been somewhat evidenced by previous literature, but with mixed results. Certainly not all individuals who have ADHD go on to have alcohol use disorder; therefore there must be other factors influencing this relationship. More research remains to be done on confounding and moderating factors in this relationship, including genetic factors (such as familial prevalence of alcohol use disorder), and social factors (such as relationships with family, friends, and teachers). These factors, if proven to be valid confounders and moderators, may be considered as red flags for predicting possible AUD, and if modifiable, targets for intervention. Additionally, most previous epidemiological studies focused on assessing risk associated with one main exposure; this project is unique because it focuses on the joint effects of two childhood exposures, childhood maltreatment or neglect and ADHD symptoms.

Only a handful of previous studies have accounted for both childhood maltreatment and ADHD symptoms while predicting alcohol and drug use disorders. Individuals with ADHD are more likely to be victims of child maltreatment and also more likely to develop alcohol use disorder, but these three variables are rarely considered together in epidemiological studies. One small study of 86 individuals diagnosed with ADHD showed that maltreatment predicted substance use disorders in this population even after controlling for SES and conduct disorder (De Sanctis et al., 2008). Overall, this is a largely unexplored area of study. Similarly, the variable of parental AUD is not always included in statistical models; for example, Huang et al did not include parental AUD when addressing the association between childhood

maltreatment and adult drug use, even though they were using the Add Health dataset (where parental AUD variables are available) and even though they included other, less relevant family characteristics such as family member suicide (Huang et al., 2011). Thus this study attempts to improve upon the existing literature by including these important family and individual characteristics. Finally, using self-reported ADHD symptoms rather than clinical diagnosis of ADHD allows for a more sensitive method of capturing life stress due to these symptoms in subclinical patients.

Therefore, these three studies will add to the existing literature in the abovementioned ways, having important implications for the cumulative effects of stressful events in childhood and treatment of adulthood disorders, as well as potential intervention targets in adolescence, in order to provide more knowledge on adulthood AUD and obesity as well as potential methods for reduction. This research uses a nationally representative, longitudinal dataset in an attempt to improve upon previous literature in ways such as identifying additional variables that may act as confounders, mediators, or effect modifiers, as well as exploring multiple definitions of variables such as obesity and how the associations with childhood experiences change as a result. Papers 1 and 2 (Chapters 3-4) will also have implications for epidemiological researchers, regarding a robust and informative method to quantify the indirect effects of a mediating variable.

Chapter 2: Methods

The following chapter contains additional detailed information about the epidemiological methods and principles used, in addition to what is presented in Chapters 3-5.

2.1. Detailed information about study design

2.1.1. Overall Study Design

The overall study design of this project was secondary data analysis of a longitudinal cohort study with four waves of data collection. This project was approved by the University of Maryland Institutional Review Board.

2.1.2. Data Source

The National Longitudinal Survey of Adolescent to Adult Health (Add Health) is a nationally representative cohort study following almost 20,000 participants from adolescence into early adulthood. The study was designed and conducted by the Carolina Population Center at the University of North Carolina, Chapel Hill. A multistage stratified cluster design was used to sample 7th-12th grade students from 80 high schools and 52 middle schools in the U.S. in 1994 and 1995. Additional details of the Add Health study design can be found on the Add Health website

(<http://www.cpc.unc.edu/projects/addhealth>; UNC Carolina Population Center, 2011).

The present study uses data from Wave I (collected in 1994-1995; mean age 15 years), Wave III (2001-2002; mean age 21 years), and Wave IV (2008-2009; mean age 28 years). Data was collected using in person interview, as well as computer-assisted self-interview for sensitive questions.

2.1.3. Participants and Criteria for Selection

In the Add Health dataset, 12,288 participants have data and sample weights for Waves I, III, and IV. Cases were excluded from analyses if they were missing data for the exposure variable, mediating variables, or the outcome variable.

2.1.4. Variables of Interest

2.1.4.1. Childhood maltreatment and neglect

Maltreatment experience (physical and sexual) before entering sixth grade was assessed with two retrospective questions: *“How often had your parents or other adult care-givers slapped, hit, or kicked you?”* and *“How often had one of your parents or other adult care-givers touched you in a sexual way, forced you to touch him or her in a sexual way, or forced you to have sexual relations?”* Reporting one or more occurrences of physical maltreatment was coded as “physical maltreatment” (1) for having experienced some physical maltreatment; reporting no occurrences was coded as “no physical maltreatment” (0; referent). Sexual maltreatment was coded in the same way. Adult participants retrospectively responded to questions regarding childhood maltreatment at Wave III, because of ethical concerns surrounding mandatory reporting of child maltreatment. Because of the sensitive nature of the questions, the questions were administered using computer-assisted self-interviewing.

Neglect was measured with two retrospective questions: *“By the time you started sixth grade, how often had your parents or other adult care-givers left you home alone when an adult should have been with you?”* (supervisory neglect) and *“How often had your parents or other adult care-givers not taken care of your basic needs, such as*

keeping you clean or providing food or clothing?” (physical neglect). Following previous researchers’ work with the Add Health dataset, participants who reported more than 5 instances of being left home alone and/or at least 1 instance of neglecting basic needs were coded as experiencing childhood neglect (Fang & Corso, 2007).

Finally, an overall “any maltreatment” variable was constructed, with those reporting any physical maltreatment, any sexual maltreatment, and/or any neglect coded as 1 (any maltreatment), and those reporting none of the maltreatment types as 0 (no maltreatment).

This measure of maltreatment has been used by other researchers (Fletcher, 2009; Shin et al., 2009). In general, retrospective self-report of child maltreatment is considered to be a valid measure, with fair to moderate test-retest reliability; one study reported a kappa of 0.41 for retrospective self-report of childhood physical abuse (McKinney et al., 2009). There’s a chance that retrospective self-report may miss some cases of individuals who do not remember their experiences or may be reluctant to report them as adults (Barnett et al., 2005). However, no measure of childhood maltreatment is perfect; using only cases substantiated by a court or Child Protected Services excludes cases that are unproven, less severe or never reported. Therefore self-reported experiences of childhood maltreatment on a nationally representative survey such as Add Health may be the highest quality data available.

2.1.4.2. ADHD symptoms

ADHD symptoms were assessed retrospectively at Wave III with 17 questions about the respondent's behavior between 5 and 12 years of age, dichotomized into two domains, hyperactivity/impulsivity (HI) and inattention (IN), as follows:

Questions about hyperactivity and impulsivity (HI): "When you were between 5 and 12..."

1. ... you fidgeted with your hands or feet or squirmed in your seat.
2. ... you left your seat in the classroom or in other situations when being seated was expected.
3. ... you felt restless.
4. ... you had difficulty doing fun things quietly.
5. ... you felt "on the go" or "driven by a motor."
6. ... you talked too much.
7. ... you blurted out answers before the questions had been completed.
8. ... you had difficulty awaiting your turn.

Questions about inattention (IN): "When you were between 5 and 12..."

1. ... you failed to pay close attention to details or made careless mistakes in your work.
2. ... you had difficulty sustaining your attention in tasks or fun activities.
3. ... you didn't listen when spoken to directly.

4. ... you didn't follow through on instructions and failed to finish work.
5. ... you had difficulty organizing tasks and activities.
6. ... you avoided, disliked, or were reluctant to engage in work requiring sustained mental effort.
7. ... you lost things that were necessary for tasks or activities.
8. ... you were easily distracted.
9. ... you were forgetful.

Wording and choice of questions reflected DSM-IV criteria for clinician diagnosis of ADHD, with two exceptions. The DSM-IV impulsivity symptom of "Often interrupts or intrudes on others (e.g., butts into conversations or games)" was not included on the Add Health questionnaire. "You were spiteful or vindictive" was asked instead, which is not a DSM-IV symptom and therefore was excluded from current analyses, resulting in a total of 8 HI symptoms and 9 IN symptoms. Each question had the following response options: never or rarely (0), sometimes (1), often (2), or very often (3). Following the precedent set by Kollins et al., 2005, respondents were coded as reporting a symptom present if they answered often (2) or very often (3). A six symptom cutoff was used for each domain, consistent with DSM-IV criteria. For analyses, respondents were coded as meeting criteria for at least one ADHD domain, or neither domain.

The internal consistency and validity of the ADHD items and scales from the Add Health sample has been reported previously. Internal consistency was found to be adequate (Cronbach $\alpha = 0.86$), and individuals whose parents reported > 6 items on the

IN and/or HI scales were more likely to have reported learning/behavioral problems at Wave I, and more likely to report taking medication for ADHD at Wave III (Kollins et al., 2005).

2.1.4.3. Body mass index and obesity

Body mass index (BMI) is the most commonly used indicator of body fat, due to the fact that it is inexpensive and easy to calculate using just height and weight. Other measures such as dual energy x-ray absorptiometry (DXA) may be more precise or reliable, but require expensive equipment and trained staff to measure each participant. BMI is better suited for surveys such as Add Health due to ease of measurement. BMI has been shown to be related to all-cause mortality (Carmienke et al., 2013) and is therefore an important indicator of body fat and general health.

Participants were asked to self-report their height in feet and inches, and weight in pounds. The following formula was used to calculate both adolescent (Wave I) and adult (Wave IV) BMI:

$$\text{BMI} = \text{mass}(\text{kg})/\text{height}(\text{m})^2 = [\text{mass}(\text{lbs})/\text{height}(\text{in})^2] \times 703$$

Typically, clinicians and researchers use BMI to classify individuals into weight status categories as follows: underweight ($<18.5 \text{ kg/m}^2$), normal weight ($18.5\text{-}24.9 \text{ kg/m}^2$), overweight ($25\text{-}29.9 \text{ kg/m}^2$), and obese ($\geq 30 \text{ kg/m}^2$). These categories are consistent with current CDC guidelines. We used a dichotomous variable: not obese ($<30 \text{ kg/m}^2$) and obese ($\geq 30 \text{ kg/m}^2$). These measures of body mass index and obesity have been used previously in this field of research (Midei & Matthews, 2011). Additionally,

we further categorized moderate obesity (<35 vs. ≥ 35 kg/m²), and extreme obesity (<40 vs. ≥ 40 kg/m²).

In addition, the Add Health dataset includes a variable that measures self-rated weight status. The question asks, “*How do you think of yourself in terms of weight?*” Possible answers include: very underweight, slightly underweight, about right, slightly overweight, or very overweight.

2.1.4.4. Alcohol use disorder

The Add Health dataset included many questions about use, frequency, amount, and consequences of alcohol consumption at Wave IV. Several of these questions were used by the Add Health team to construct a variable measuring lifetime alcohol abuse and dependence. These questions were based on DSM-IV criteria, which are the gold standard for diagnosis of alcohol abuse and dependence. Questions included the following (answer options in parentheses):

Abuse:

1. How often has your drinking interfered with your responsibilities at work or school? (never, one time, more than one time)
2. How often have you been under the influence of alcohol when you could have gotten yourself or others hurt, or put yourself or others at risk, including unprotected sex? (never, one time, more than one time)

3. How often have you had legal problems because of your drinking, like being arrested for disturbing the peace or driving under the influence of alcohol, or anything else? (never, one time, more than one time)
4. How often have you had problems with your family, friends, or people at work or school because of your drinking? (never, one time, more than one time)
5. Did you continue to drink after you realized drinking was causing you problems with family, friends, or people at work or school? (yes/no)

Dependence: (all questions are yes/no format)

1. Have you ever found that you had to drink more than you used to in order to get the effect you wanted?
2. Has there ever been a period when you spent a lot of time drinking, planning how you would get alcohol, or recovering from a hangover?
3. Have you often had more to drink or kept drinking for a longer period of time than you intended?
4. Has there ever been a period of time when you wanted to quit or cut down on your drinking?
5. When you decided to cut down or quit drinking, were you able to do so for at least one month?

6. During the first few hours of not drinking, do you experience withdrawal symptoms such as the shakes, feeling anxious, trouble getting to sleep or staying asleep, nausea, vomiting, or rapid heartbeats?
7. Have you ever continued to drink after you realized drinking was causing you any emotional problems (such as feeling irritable, depressed, or uninterested in things or having strange ideas) or causing you any health problems (such as ulcers, numbness in your hands/feet or memory problems)?
8. Have you ever given up or cut down on important activities that would interfere with drinking like getting together with friends or relatives, going to work or school, participating in sports, or anything else?

Based on their responses to the previous questions, the Add Health team classified participants into three groups: No abuse/dependence (72.6%), abuse (12.9%), or dependence with or without physiological symptoms (14.5%). Answering positively to one of the abuse symptoms, or three of the dependence symptoms (with special emphasis on tolerance and withdrawal), would classify the participant as positive for alcohol abuse and/or dependence. This variable was measured at Wave IV, when participants were between 24-32 years old; therefore this measure captures the majority of individuals who will develop alcohol use disorder, because previous literature indicates that the mean age of onset is about 22 years of age and the hazard rate of onset peaks around 19 years of age (Hasin et al., 2007).

Due to the Add Health questionnaire skip patterns, about 59.4% of the sample was not asked all of the abuse/dependence questions based on answers to previous

questions about frequency of alcohol use. These cases were considered to be very light drinkers and non-drinkers, and they were classified as no abuse/dependence for analysis purposes.

This is considered a valid measure of alcohol use disorder, because it is based on DSM-IV criteria (the gold standard for psychiatric diagnosis). A recent literature review reported strong reliability and validity of the DSM criteria for diagnosing alcohol abuse and dependence, across age, sex, and ethnic groups; test-retest reliability of lifetime alcohol dependence ranged from 0.69-0.79, and DSM diagnoses showed high concordance with ICD with kappa values between 0.71-0.92 (Hasin et al., 2006).

2.1.4.5. Adolescent depressive symptoms

Depressive symptoms were measured at Wave I during adolescence, using the “Feelings Scale” of the Add Health dataset, which is modeled closely after the widely used Center for Epidemiologic Studies Depression Scale (CES-D). The Feelings Scale includes 19 questions, with each question referring to feelings in the past week. The questionnaire begins by asking, *“These questions will ask about how you feel emotionally and about how you feel in general. How often was each of the following things true during the past week?”* The 19 questions included the following:

1. You were bothered by things that usually don’t bother you.
2. You didn’t feel like eating, your appetite was poor.
3. You felt that you could not shake off the blues, even with help from your family and friends.
4. You felt that you were just as good as other people.

5. You had trouble keeping your mind on what you were doing.
6. You felt depressed.
7. You felt that you were too tired to do things.
8. You felt hopeful about the future.
9. You thought your life had been a failure.
10. You felt fearful.
11. You were happy.
12. You talked less than usual.
13. You felt lonely.
14. People were unfriendly to you.
15. You enjoyed life.
16. You felt sad.
17. You felt that people disliked you.
18. It was hard to get started doing things.
19. You felt that life was not worth living.

Each question was coded on a scale from 0 to 3; participants responded “never or rarely” (0), “sometimes” (1), “a lot of the time” (2), or “most of the time or all of the time” (3). Reverse coding was used for #4, 8, 11 and 15, so that these questions were coded as follows: “never or rarely” (3), “sometimes” (2), “a lot of the time” (1), or “most of the time or all of the time” (0). Totals were summed over the 19 questions, and possible score totals ranged from 0 to 57. Cutoff scores of 22 for males and 24 for females were used to classify respondents as being at risk for depression during adolescence, based on cutoff scores used in previous literature (Roberts et al., 1991).

Therefore there were two methods of coding the mediator variable of depressive symptoms: 1) continuous, and 2) dichotomous, based on whether the participant met the cutoff score.

The CES-D has been commonly used as a screener for depression in epidemiological studies, and internal reliability and sensitivity have been found to be adequate in large samples of high school students (Olino et al., 2012; Roberts et al., 1991) as well as in international samples (Morin et al., 2011). One study using adolescents of different ages reported that internal consistency of the CES-D was reasonably high, with a coefficient alpha of 0.86 for the high school students (Radloff, 1991). Another study found internal consistency to also be high, with alphas from 0.84 to 0.90, and fair test-retest consistency, with a correlation of 0.57 (Radloff, 1977).

2.1.4.6. Adolescent delinquent behavior

The Add Health dataset contained a scale to measure delinquency in the last twelve months at the time of Wave I. The fifteen questions are presented below.

“In the past 12 months, how often...

1. did you paint graffiti or signs on someone else's property or in a public place?"
2. did you deliberately damage property that didn't belong to you?"
3. did you lie to your parents or guardians about where you had been or whom you were with?"
4. did you take something from a store without paying for it?"

5. did you get into a serious physical fight?”
6. did you hurt someone badly enough to need bandages or care from a doctor or nurse?”
7. did you run away from home?”
8. did you drive a car without its owner’s permission?”
9. did you steal something worth more than \$50?”
10. did you go into a house or building to steal something?”
11. did you use or threaten to use a weapon to get something from someone?”
12. did you sell marijuana or other drugs?”
13. did you steal something worth less than \$50?”
14. did you take part in a fight where a group of your friends was against another group?”
15. were you loud, rowdy, or unruly in a public place?”

The delinquency scale included questions to reflect multiple types of delinquency behavior, such as property crime (#1, 2, 4, 8, 9, 10, 13), violent crime (#5, 6, 11, 14) status offenses (#3, 7), drug sales (#12), and disturbing the peace (#15). These questions have been used previously to measure adolescent delinquency with Wave I Add Health data, although different authors have used different combinations of questions. For example, Aalsma et al. used seven of the questions (#2, 9, 10, 11, 12, 13, and 14), which

they showed to have a Cronbach's alpha of 0.76 (Aalsma et al., 2010). Armour & Haynie chose to use six questions (#1, 2, 4, 9, 12, and 13) to measure adolescent delinquency; they reported a Cronbach's alpha of 0.84 (Armour & Haynie, 2007). For this project, all 15 questions were included.

Each question had four possible answers: never, 1 or 2 times, 3 or 4 times, or 5 or more times. Following previous research, answers were dichotomized into two groups: never, or ≥ 1 time. The fifteen individual delinquency variables were summed into a total delinquency scale, which had a range from 0-15.

2.1.4.7. Adolescent alcohol consumption

Adolescent alcohol consumption at Wave I was measured with the following question: "*Do you ever drink beer, wine, or liquor when you are not with your parents or other adults in your family?*" This variable was coded dichotomously (yes or no).

2.1.4.8. Adolescent friend alcohol consumption

Adolescent friend alcohol consumption at Wave I was measured with the following question: "*Of your 3 best friends, how many drink alcohol at least once a month?*" This variable was coded as follows: no friends, one friend, two friends, or three friends.

2.1.4.9. Parental AUD

At Wave I, one of the respondent's parents was asked whether the biological mother or father of the respondent had AUD. Parental AUD was coded as having at least one biological parent with AUD.

2.1.4.10. Sex

Participants were coded as male or female.

2.1.4.11. Race/ethnicity

Race/ethnicity was self-reported at Wave III. Race/ethnicity of the participant was coded as follows: non-Hispanic White, non-Hispanic Black, Hispanic, Asian, American Indian or Native American, or Other.

2.1.4.12. Maternal education

Parental socioeconomic status (SES) was assessed by maternal education, which was coded as follows: less than high school, high school graduate or GED, some college or technical school, and college graduate or greater. These categories were used by previous Add Health researchers (Hussey et al., 2006, Ouyang et al., 2008, and Shin & Miller, 2012).

2.2. Assessment of potential biases (selection bias, information bias, and confounding bias)

2.2.1. Selection Bias

In general, selection bias is a larger concern for case control studies, when a systematic error in the ascertainment of cases and controls results in distortion of the main association of interest. Cohort studies may be vulnerable to selection bias especially when participants are selected based on an exposure status, which may be minimized by

using participants from a defined reference population. The Add Health dataset used a multistage stratified cluster design to sample students from schools all over the U.S., and incorporated sample weights for each participant. Thus selection bias should be minimized, and the results from this study should be representative of American individuals from this age cohort.

The follow-up rate was high for such a large long term study, with a rate of 80.3% at Wave IV. Thus, loss to follow-up was not of particular concern. However, researchers must always consider the possibility of differential attrition, that is, the general principle that the “sickest” individuals are most prone to loss to follow-up in a longitudinal cohort study. This may result in biased effect estimates, and should be considered when interpreting the study results. As discussed in Chapters 3-5, the prevalence of adulthood AUD and obesity in this dataset were fairly comparable to those in the general population (Centers for Disease Control, 2013; Hasin, et al., 2007), and therefore we are reasonably assured that the study population is representative of the U.S.

2.2.2. Information Bias

The researchers who conducted the Add Health study and the author both took measures to minimize misclassification of participants due to flawed data collection or analysis procedures. Quality assurance procedures used by the University of North Carolina (UNC) include using prewritten interview questions in order to minimize interviewer bias, and computer assisted self-interview (CASI) to administer sensitive questions, in order to minimize bias due to a desire to please the interviewer. However, participants may still have inaccurately answered some sensitive questions, such as those

about alcohol use. Retrospective measurement of childhood maltreatment and ADHD symptoms may also be vulnerable to some recall bias, if participants inaccurately reported their past experiences. However, these types of variables are always vulnerable to some information bias; for example, using only cases of maltreatment that were validated using court cases or other records would result in missed cases. Similarly, defining cases using clinical judgment of AUD, ADHD, depression, or other disorders results in missing subclinical cases with a more subtle presentation. Therefore, there are advantages and disadvantages to using each type of variable. The self-reported variables are a more sensitive way of measuring these variables. When possible, multiple ways of defining variables were explored (such as testing multiple cutoff points for depressive symptoms, multiple domains of ADHD symptoms, etc.).

Adolescent and adult body mass index was calculated using self-reported height and weight, which is vulnerable to reporting bias. For example, participants may not know their current weight, or they may report inaccurate measurements due to embarrassment or a desire to be a different weight. The gold standard measurement would be height and weight measurements performed by the interviewer; however, this measurement requires more time to perform, increasing burden for the interviewer and participant. Self-reported height and weight have been shown to be a reliable proxy measure when direct measurement is not practical, using a diverse sample of 24,221 adolescents participating in the School Physical Activity and Nutrition (SPAN) surveillance system in Texas; although adolescents tended to overestimate height and underestimate weight, the difference in self-reported vs. objectively measured BMI was

only -0.23 to -0.7 kg/m² (Perez et al, 2015). Therefore, self-reported height and weight may be vulnerable to some bias, but are still a reliable way to calculate body mass index.

2.2.3. Confounding Bias

In epidemiological studies, there is a concern that spurious factors (confounders) can influence the direction and/or magnitude of the association of interest either towards or away from the null. Statistical adjustment using multivariate analysis is a method to estimate the main association of interest while controlling for one or more confounding variables. In this project, each study included assessment of potential confounding variables based on previous literature, such as age, sex, parental socioeconomic status (measured by maternal education and a functional outcome, trouble paying bills), parental AUD, and child maltreatment and neglect. Thus the confounding effect of these variables is reduced via statistical adjustment in the models. Confounders were carefully selected for final adjusted models based on the change in the effect estimate of the main association, strength of association between the confounder and the exposure and outcome variables, and theoretical importance based on previous literature. Even after statistical adjustment, there is always some potential for residual confounding in epidemiological studies, such as confounding by variables that have not been measured, or imprecise or inaccurate measurement of a variable.

2.3. Statistical approaches to test hypotheses

Logistic regression (PROC SURVEYLOGISTIC, SAS software version 9.3) was used to test the study hypotheses and estimate the main associations of interest by

calculating odds ratios and 95% confidence intervals, and predicted probabilities. Sample weights were applied to all analyses to account for the complex sample design, using the Wave IV strata, cluster and weight variables provided by the UNC Add Health team.

2.4. Assessment of potential mediation effects or/and interaction effects

The presence of moderation (multiplicative interaction) was assessed by assessment of homogeneity of stratum-specific effect estimates, testing of interaction terms in regression models, and comparison of observed and expected joint effects, as described in Szklo & Nieto, 2007. The expected joint effects were calculated by the formula $OR_{A+Z-} * OR_{A-Z+}$.

Mediation was tested using the method described in MacKinnon (2008). This method is similar to the classical method described in Baron & Kenny (1986), but improves upon the classical method because of the specification of a way to quantify mediation, rather than just test whether it is present. The MacKinnon method involves fitting three models, where Y is the outcome, X is the exposure, and M is the mediator:

$$1) Y = i_1 + cX + e_1$$

$$2) Y = i_2 + c'X + bM + e_2$$

$$3) M = i_3 + aX + e_3$$

These three equations describe three parts of the theoretical description of mediation: 1) the exposure is associated with the outcome, 2) the mediator is associated with the outcome while controlling for the exposure, and 3) the exposure is associated

with the mediator. This is very similar to the classic method of Baron & Kenny, except that the second statement requires not only that the mediator is associated with the outcome, but also that it must be associated with the outcome while controlling for the exposure.

Mediation analysis therefore included three logistic regression analyses to test each mediator (“single mediator models”). The indirect effect of mediation was calculated with the equation ab , and the proportion of total effect mediated was calculated with the equation ab/c (MacKinnon, 2008). This equation reflects the fact that mediation depends on the extent to which the independent variable changes the mediator, a , and the extent to which the mediator affects the outcome variable, b ; therefore, the product of a and b reflects the mediated effect. This method is relatively new but has been used in recent public health research (De Cocker et al., 2015). Another final mediation analysis was conducted with two statistically significant mediator variables (“multiple mediator model”), using the following models:

$$1) Y = i_1 + cX + e_1$$

$$2) Y = i_2 + c'x + b_1M_1 + b_2M_2 + e_2$$

$$3) M_1 = i_3 + a_1x + e_3$$

$$4) M_2 = i_4 + a_2x + e_4$$

In the formulas above, a_1 is the parameter relating the independent variable to the first mediating variable, a_2 is the parameter relating the independent variable to the second mediating variable, b_1 and b_2 are the parameters relating the first and second

mediators to the dependent variable adjusted for the effects of the independent variable, c represents the relation between the independent variable to the dependent variable, and c' represents the relation between the independent variable to the dependent variable adjusted for the effects of the mediators (MacKinnon, 2008, pages 49-50). The indirect effect of mediation was calculated by the equation $a_1b_1+a_2b_2$, and the proportion of total effect mediated calculated by the equation $(a_1b_1+a_2b_2)/c$. Finally, a fully adjusted multiple mediator model included adjustment for confounders.

2.5. Model specification

Sex, race/ethnicity, parental AUD, maternal education, and childhood maltreatment were included as confounders in analyses when appropriate. Additional potential confounders were also considered, such as age at Wave I, parental socioeconomic status (trouble paying bills), and household structure (number of biological parents living with child).

Potential confounders were tested by adding individual variables to the model one at a time and observing the effect on the association of interest. The selection of confounders to be included in the final fully adjusted model was based on the size of the change in the association of interest and theoretical importance based on previous literature.

2.6. Assessment of model assumptions

The logistic regression model has the assumption that the independent variables should not be highly correlated with each other, or the effect estimate may be biased. Therefore, variables were tested for multicollinearity, and variables that were highly correlated were not included in a regression model together. It is also assumed that there are no omitted influences, i.e., no important variables have been omitted from the model. Although there is no way to definitively ensure the inclusion of every important variable, we attempted to look at many potential confounders based on prior literature and theoretical importance, such as two measures of parental socioeconomic status (maternal education and trouble paying bills). Potential confounders that were not found to significantly contribute to the model were omitted from the analyses.

There are a couple of additional assumptions and considerations regarding the mediation analysis in Chapters 3-4. One assumption is that of temporal precedence; X must come before M, which must come before Y. This assumption is met by our mediation analyses, because childhood factors (X) occur before age 12, adolescent factors (M) occur at Wave I in adolescence at a mean age of 15, and adult factors (Y) occur at Wave IV. Another consideration is that mediation attempts to reflect true causal relations between variables; however, in the strictest sense, only random assignment of X could truly establish causal relations. Therefore, this observational research cannot definitively determine causation between X, M, and Y (MacKinnon, 2008). However, given the nature of the exposure variables (ADHD symptoms and childhood maltreatment), experimental study designs would not be appropriate. In addition, the temporal sequence between the childhood factors, adolescent factors, and adult factors is

known. Therefore, although our study designs are observational rather than experimental, and therefore the results may suggest causation but may not definitely prove causation, we believe the results are still highly informative.

2.7. Limitations of the study

As with any research study, especially a secondary data analysis of an existing dataset, there are some limitations to the study methods. The variables of childhood maltreatment and ADHD symptoms were measured retrospectively and therefore may be vulnerable to some measurement/recall bias, if participants inaccurately reported their past experiences. The questionnaire was designed to encourage participation, i.e., using computer assisted self-interview for sensitive questions such as maltreatment experience; however, 1,394 participants had missing data for at least one maltreatment variable or body mass index at Wave IV. Based on the sensitivity of the question, we cannot assume that a missing answer is either a negative or positive answer. We note that participants who were missing one maltreatment variable were slightly less likely to report other types of maltreatment, which is logical given their reluctance to answer at least one of the maltreatment questions. The participants with missing maltreatment data also had a lower proportion of obesity (32.7% vs. 37.2%) and extreme obesity (6.6% vs. 9.2%) than others. The participants with missing data were slightly more likely to be male and non-White than others. In order to take a conservative approach, these cases were excluded from analyses for Paper 1. Although more sophisticated methods for handling missing data exist, such as multiple imputation, we note that these data are not missing at random, which may violate an assumption of the SAS multiple imputation procedures (Yuan,

2000). Regarding Papers 2-3, participants were similarly excluded if they were missing data for maltreatment or AUD at Wave IV (n=1,250). The excluded participants did not have a statistically significant difference in proportion of ADHD, AUD, or parental AUD. To maintain the validity of the sample weights in the complex survey design, domain analysis was used for all subgroup analyses (including exclusion of participants with missing data) rather than a BY statement. This is essential to produce statistically correct standard errors for subgroup analyses (Berglund, 2009).

Another limitation of this project is the difficulty in determining the order or timing of the two variables, ADHD symptoms (asked about the period between 5-12 years of age) and childhood maltreatment (asked about the period before entering sixth grade, when students are generally between 11-12 years of age). It's likely that for some children, maltreatment or neglect can indirectly lead to later behaviors that mimic symptoms of ADHD, such as nervousness or difficulty sustaining attention on schoolwork. For others, ADHD symptoms cause acting out at home and a higher chance of getting into trouble and possibly being physically maltreated. Therefore this relationship may be somewhat bidirectional; the temporal relationship between these two variables should be further explored in future studies. Finally, as discussed previously, the observational nature of the dataset means that the associations reported may suggest causation but may not definitively prove causation between the variables under study (although experimental study designs are not appropriate for studying the associations of interest).

Despite the above limitations, this study has a number of strengths as well. The National Longitudinal Study of Adolescent to Adult Health is a large, nationally

representative dataset with a large sample size and a longitudinal design following participants from adolescence to adulthood. The analyses are weighted using the sample weights provided, meaning that the conclusions may be representative of the general American population for this cohort. A robust method of mediation analysis was used which offers improvements over the classical method of mediation analysis, including quantitative measurement of mediation and hypothesis testing ability.

Chapter 3 (Paper 1): The Pathway from Childhood Maltreatment to Adulthood Obesity, Mediated by Adolescent Depressive Symptoms and BMI

Purpose

To examine the association between childhood maltreatment and adulthood obesity, and mediating effects of adolescent depressive symptoms and BMI.

Methods

This study used data from the National Longitudinal Study of Adolescent to Adult Health (n=10,894). Logistic regression was used to examine associations between childhood maltreatment and obesity in adulthood, as measured by BMI and self-related weight status. Mediation by adolescent depressive symptoms and adolescent BMI was tested.

Results

Individuals who reported sexual maltreatment were 34% more likely to be obese (BMI \geq 30; odds ratio, OR=1.34, 95% CI: 1.05-1.72) and 72% more likely to be extremely obese (BMI \geq 40) in adulthood (AOR=1.72, 95% CI: 1.18-2.51) than those who did not report sexual maltreatment. Individuals who reported physical maltreatment were 37% more likely to be extremely obese than those who did not report physical maltreatment (AOR=1.37, 95% CI: 1.11-1.70). Adolescent depressive symptoms and adolescent BMI were statistically significant mediators in the relationships between sexual and physical

maltreatment and extreme obesity ($p's < .05$). Physical maltreatment was associated with self-rated weight status in adulthood ($OR=1.27$, 95% CI: 1.06-1.52), but sexual maltreatment was not. Adolescent depressive symptoms and BMI were again statistically significant mediators between physical maltreatment and self-rated obesity ($p's < .05$).

Conclusions

The association between physical and sexual maltreatment in childhood and extreme obesity in adulthood was partially mediated by adolescent depressive symptoms and BMI. Further research is needed to explore these mechanisms and interventions for maltreatment victims.

Keywords: Maltreatment, Obesity, Depression, Adolescent Health

3.1. Introduction

According to the CDC, more than a third of American adults today are obese, representing a drastic increase since 1990. Obesity is associated with chronic health conditions such as sleep apnea and osteoarthritis; it can also reduce life expectancy due to increased risk of serious health conditions such as heart disease, stroke, diabetes and certain types of cancer. Obesity is related to increased medical costs; the CDC estimates that in 2008, medical costs related to obesity could have risen to \$147 billion, or almost 10% of all medical spending in the U.S. (Centers for Disease Control, 2013). Thus, obesity is a dangerous condition that is highly prevalent in American society today. Research that analyzes potential causes or risk factors of obesity is critical to recognizing at-risk individuals, and designing interventions for children, adolescents, and adults, to prevent and reduce the rate of obesity and its associated health outcomes.

Some previous literature has shown that childhood maltreatment may be associated with later risk of obesity. Dube (2010) analyzed data from the Behavioral Risk Factor Surveillance System (BRFSS) from 5,378 adults living in Texas, and found that those who experienced childhood abuse and household dysfunction were 1.3 times more likely to be obese in adulthood than those who did not (Dube, Cook, & Edwards, 2010). A meta-analysis of 36 studies showed that childhood interpersonal violence, including physical abuse, sexual abuse, and peer bullying, was positively associated with risk for obesity and central adiposity (Midei & Matthews, 2011). Another recent meta-analysis of 41 studies with a total of 190,285 participants showed that childhood maltreatment was associated with elevated risk of obesity (odds ratio=1.36, 95% CI: 1.26-1.47), and this association was significant for physical maltreatment, sexual maltreatment, emotional

abuse, and physical neglect, but not emotional neglect (Danese & Tan, 2014).

Furthermore, an association has been shown between child maltreatment and health conditions such as Type 2 Diabetes due to higher body mass index (Rich-Edwards, et al., 2010).

Maltreatment's association with later obesity has been shown with multiple demographic groups. For example, data from the Black Women's Health Study showed that women who were exposed to child/teenage physical and sexual abuse were 1.29 times more likely (95% CI: 1.20-1.38) to have a body mass index (BMI) over 30; this relative risk decreased to 1.14 (95% CI: 1.08-1.21) after controlling for reproductive history, diet, physical activity, depressive symptoms, and SES (Boynton-Jarrett, et al., 2012). In addition, the association between child maltreatment and obesity may be apparent as early as adolescence. In a retrospective study of 1,434 youths admitted to an inpatient psychiatric facility, a reported history of sexual abuse was associated with BMI above the 85th percentile (odds ratio=1.41); however, physical abuse was not associated with BMI (Keeshin, et al., 2013). However, more research is needed to further explore the moderating effects of demographic variables, such as sex.

One study, by Shin & Miller, used the Add Health dataset to study the association between child maltreatment and obesity. Using latent curve modeling, they showed that childhood neglect was associated with a faster average rate of BMI growth per year compared to children who were not neglected ($p < .01$). Sexual abuse was also associated with faster rate of BMI growth ($p < .05$). The authors controlled for sex, race/ethnicity, SES, breastfeeding, depression in adolescence, relationship with parents, and parental obesity. They concluded that maltreatment was positively associated with BMI

trajectories into adulthood, possibly due to elevating daily stress, using food as a coping mechanism, or by the promotion of unhealthy behaviors as a consequence of limited supervision (Shin & Miller, 2012).

The Add Health study by Shin & Miller statistically controlled for sex as a confounder, rather than testing sex for effect modification. Sex is an important potential effect modifier to include in analyses, because males and females are different in several key ways. First, males are more susceptible to different types of maltreatment than females (e.g. males are more at risk for physical abuse and less at risk for sexual abuse than females). Second, females and males have different physiology as regards to metabolism and hormone levels, which both affect body mass index. Third, females and males may use different methods of coping with stress, such as overeating. Therefore, the present study treated sex as an effect modifier, which has not been done by many previous authors. One study that tested sex as an effect modifier used data from a sample of 464 adolescents living in Los Angeles, and reported that sexual and physical abuse were associated with higher odds of obesity for females, but not for males (Schneiderman, et al., 2012). The current study tested effect modification by sex with a larger, nationally representative dataset.

There has not been much literature assessing potential mechanisms between childhood maltreatment and later obesity. Depressive symptoms are sometimes controlled for as a confounding variable, but not often treated as a mediating variable. However, it is evident that childhood maltreatment is moderately associated with adolescent depressive symptoms (Hussey, Chang, & Kotch, 2006), which are then in turn associated with risk factors for obesity such as poor diet and lack of physical exercise (Hoare, et al., 2014).

Individuals who are mistreated in childhood are more likely to struggle with low self-esteem and feelings of self-worthlessness, which can lead to developing inappropriate coping mechanisms, such as overindulging in food. Therefore, depressive symptoms are an often overlooked but logical mediator on the pathway between childhood maltreatment and adulthood obesity. Additionally, given that poor dietary and exercise habits often begin in adolescence and persist into adulthood, childhood or adolescent body mass index is a fair predictor of adult obesity and related health problems (Kelsey, et al., 2014), and may also lie on the causal pathway between childhood maltreatment and adult obesity. Therefore, depressive symptoms and body mass index in adolescence are potential mediators in the association between maltreatment and obesity.

The objective of this study was to address gaps in the literature by investigating the association between childhood maltreatment and adulthood obesity, as measured by body mass index as well as self-reported weight status, and potential mediators including adolescent depressive symptoms and adolescent body mass index. We used a rigorous mediation analysis technique that allows for statistical testing of single and multiple mediator models (MacKinnon, 2008). We hypothesized that childhood maltreatment would be positively associated with adult obesity, that the main association would differ by sex, and that depressive symptoms in adolescence and body mass index in adolescence would each at least partially mediate the association.

3.2. Material and Methods

3.2.1. Dataset

This study was a secondary data analysis of Waves I, III, and IV of the National Longitudinal Study of Adolescent to Adult Health, the methods of which can be found on the Add Health website (UNC, 2011). The Add Health study used a multistage stratified cluster design and included four waves of data collection from adolescents to adulthood. Data were collected using in person interview, as well as computer-assisted self-interview for sensitive questions. In total, 12,288 participants had data and sample weights for Waves I (mean age 15.4), III (mean age 21.8), and IV (mean age 28.3). Cases were excluded from analyses if they were missing data for the independent variable, moderator, or outcome variable, leaving an analytic sample size of 10,894.

3.2.2. Dependent variable

Body mass index (BMI) at Waves I and IV was calculated using self-reported height in feet and inches, and weight in pounds. The following formula was used:

$$\text{BMI} = [\text{mass}(\text{lbs})/\text{height}(\text{in})^2] \times 703$$

BMI was first categorized by the Add Health study team as follows: underweight ($<18.5 \text{ kg/m}^2$), normal weight ($18.5\text{-}24.9 \text{ kg/m}^2$), overweight ($25\text{-}29.9 \text{ kg/m}^2$), obese ($30\text{-}34.9 \text{ kg/m}^2$), moderately obese ($35\text{-}39.9 \text{ kg/m}^2$), and extremely obese ($\geq 40 \text{ kg/m}^2$). These categories are consistent with current CDC guidelines. A dichotomous variable was calculated as follows: not obese ($<30 \text{ kg/m}^2$) and obese ($\geq 30 \text{ kg/m}^2$). These measures of body mass index and obesity have been used previously in this field of research (Midei & Matthews, 2011). In addition, moderate obesity was calculated as follows: not moderately obese ($<35 \text{ kg/m}^2$), and moderately obese ($\geq 35 \text{ kg/m}^2$). Extreme obesity was classified as follows: not extremely obese ($<40 \text{ kg/m}^2$), and extremely obese ($\geq 40 \text{ kg/m}^2$).

Self-rated weight status was measured using the following question: “How do you think of yourself in terms of weight?” Possible answers included very underweight, slightly underweight, about right, slightly overweight, or very overweight.

3.2.3. Independent variable

Maltreatment experience (physical and sexual) before entering sixth grade was assessed with two retrospective questions: “How often had your parents or other adult care-givers slapped, hit, or kicked you?” and “How often had one of your parents or other adult care-givers touched you in a sexual way, forced you to touch him or her in a sexual way, or forced you to have sexual relations?” Reporting one or more occurrences of physical maltreatment will be coded as “physical maltreatment” (1) for having experienced some physical maltreatment; reporting no occurrences will be coded as “no physical maltreatment” (0; referent). Sexual maltreatment was coded in the same way. Adult participants retrospectively responded to questions regarding childhood maltreatment at Wave III, because of ethical concerns surrounding mandatory reporting of child maltreatment. Because of the sensitive nature of the questions, the questions were administered using computer-assisted self-interviewing.

Neglect was measured with two retrospective questions: “By the time you started sixth grade, how often had your parents or other adult care-givers left you home alone when an adult should have been with you?” (supervisory neglect) and “How often had your parents or other adult care-givers not taken care of your basic needs, such as keeping you clean or providing food or clothing?” (physical neglect). Following previous researchers’ work with the Add Health dataset, participants who reported more than 5

instances of being left home alone and/or at least 1 instance of neglecting basic needs were coded as experiencing childhood neglect (Fang & Corso, 2007).

An overall “any maltreatment” variable was constructed, with those reporting any physical maltreatment, sexual maltreatment, and/or neglect coded as 1 (any maltreatment) and those reporting none of the maltreatment types as 0 (no maltreatment).

3.2.4. Potential Confounders and Mediating Variables

Participant age at Wave I, race/ethnicity, sex, and parental SES were tested as confounders in analyses. Self-reported race/ethnicity of the participant was coded as follows: non-Hispanic White, non-Hispanic Black, Hispanic, Asian, or Other. Parental socioeconomic status (SES) was assessed by maternal education, which was coded as follows: less than high school, high school graduate or GED, some college or technical school, and college graduate or greater. This method of categorization has been used in previous research (Hussey, Chang, & Kotch, 2006; Ouyang, et al., 2008; Shin & Miller, 2012).

Depressive symptoms were measured at Wave I during adolescence (average age 15.4 years), using the “Feelings Scale” of the Add Health dataset, which is modeled closely after the widely used Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977). The Feelings Scale includes 19 questions that ask about feelings in the past week. Each question was coded on a scale from 0 to 3; participants responded “never or rarely” (0), “sometimes” (1), “a lot of the time” (2), or “most of the time or all of the time” (3). Reverse coding was used for questions #4, 8, 11 and 15, so that these questions were coded as follows: “never or rarely” (3), “sometimes” (2), “a lot of the time” (1), or

“most of the time or all of the time” (0). Totals were summed over the 19 questions, and possible score totals ranged from 0 to 57. Cutoff scores of 22 for males and 24 for females were used to classify respondents as being at risk for depression during adolescence, based on cutoff scores used in previous literature (Roberts, Lewinsohn, & Seeley, 1991).

3.2.5. Statistical analysis

SAS software version 9.3 (Cary, NC) was used for all analyses. Sample weights were applied to all analyses to account for the complex sample design. Participants with missing data for the independent, moderating, or outcome variables were excluded from analyses. Independent missing categories of each confounder were created to account for missing data for race/ethnicity (0.3%), and maternal education (12.1%). PROC SURVEYLOGISTIC (SAS software version 9.3) was used to estimate odds ratios and predicted probabilities. Logistic regression models were calculated for the outcome variable, obesity, in three ways: BMI \geq 30 vs. BMI<30, BMI \geq 35 vs. BMI<35, and BMI \geq 40 vs. BMI<40. Predicted probabilities were calculated when the prevalence of the outcome was greater than 10%. Adjusted models were constructed with the following confounders: sex, race/ethnicity, and maternal education. Moderation by sex was tested for each model.

To test for the mediating effect of adolescent depressive symptoms and adolescent body mass index, the method described in MacKinnon (2008) was used. This method is similar to the classical method described in Baron & Kenny (1986), but improves upon this method because of the inclusion of a way to quantify mediation, rather than just test

whether it is present. The MacKinnon method involves testing three equations, where Y is the outcome (obesity), X is the exposure (child maltreatment), and M is the mediator (depressive symptoms):

$$1) Y = i_1 + cX + e_1$$

$$2) Y = i_2 + c'X + bM + e_2$$

$$3) M = i_3 + aX + e_3$$

These three equations describe three parts of the theoretical description of mediation: 1) the exposure is associated with the outcome, 2) the mediator is associated with the outcome while controlling for the exposure, and 3) the exposure is associated with the mediator. This is very similar to the classic method of Baron & Kenny, except that the second statement requires not only that the mediator is associated with the outcome, but also that it must be associated with the outcome while controlling for the exposure.

Mediation analysis therefore included three logistic regression analyses to test each mediator (“single mediator models”). The effect of mediation was calculated with the equation $a*b$ (MacKinnon, 2008). This method is relatively new, but has been used in recent public health research (De Cocker, et al., 2015). Another final regression analysis was conducted with both mediator variables (“multiple mediator model”) using the following models:

$$1) Y = i_1 + cX + e_1$$

$$2) Y = i_2 + c'X + b_1M_1 + b_2M_2 + e_2$$

$$3) M_1 = i_3 + a_1X + e_3$$

$$4) M_2 = i_4 + a_2X + e_4$$

In the formulas above, a_1 is the parameter relating the independent variable to the first mediating variable, a_2 is the parameter relating the independent variable to the second mediating variable, b_1 and b_2 are the parameters relating the first and second mediators to the dependent variable adjusted for the effects of the independent variable, c represents the relation between the independent variable to the dependent variable, and c' represents the relation between the independent variable to the dependent variable adjusted for the effects of the mediators (MacKinnon, 2008). The indirect effect of mediation was calculated by the equation $a_1b_1+a_2b_2$, and the proportion of total effect mediated calculated by the equation $(a_1b_1+a_2b_2)/c$.

3.3. Results

3.3.1. Descriptive statistics

Descriptive statistics for the sample can be found in Table 1. At Wave IV, 4,057 participants met criteria for obesity ($BMI \geq 30$; 37.3%), 2,046 participants met criteria for moderate obesity ($BMI \geq 35$; 18.9%) and 1,020 participants met criteria for extreme obesity ($BMI \geq 40$; 9.2%). These prevalences are comparable to those previously reported; the CDC estimated a national obesity prevalence of 34.9% in 2012 (Centers for Disease Control, 2013). The breakdown for each weight class was as follows (not shown in table): 151 (1.4%) underweight ($BMI < 18.5$), 3,421 (32.2%) normal (BMI 18.5-25), 3,265 (29.1%) overweight (BMI 25-30), 2,011 (18.5%) obese (BMI 30-35), 1,026 (9.7%)

moderately obese (BMI 35-40), and 1,020 (9.2%) extremely obese (BMI \geq 40). Regarding childhood maltreatment, 37.9% of participants reported any maltreatment, 28.3% reported physical maltreatment, 4.8% reported sexual maltreatment, and 19.5% reported neglect. A greater percentage of participants who reported maltreatment met criteria for extreme obesity, for each type of maltreatment; however, this difference was only significant for sexual maltreatment (7.8% vs. 4.5%; $p=.001$) and any maltreatment (42.7% vs. 37.5%; $p=.02$). Participants who met criteria for extreme obesity were also more likely to be female and non-White, more likely to report adolescent depressive symptoms, and had a higher mean BMI at Wave I.

3.3.2. *Associations between Maltreatment and Obesity*

Table 2 shows the unadjusted associations between types of maltreatment and adult obesity as measured by BMI. Regarding the association between maltreatment and obesity defined as BMI \geq 30 kg/m², only sexual maltreatment was significantly associated with adult obesity. Those who reported sexual maltreatment had a greater predicted probability (44.0% vs. 37.0%; $p<.0001$) and greater odds (OR=1.34, 95% CI: 1.05-1.72) of obesity than those who did not report sexual maltreatment. Defining moderate obesity as BMI \geq 35, physical maltreatment (predicted probabilities 20.9% vs. 18.0%, $p<.0001$; OR=1.20, 95% CI: 1.01-1.43) and sexual maltreatment (24.3% vs. 18.6%, $p<.0001$; OR=1.40, 95% CI: 1.03-1.90) were significantly associated with moderate obesity. When the obesity outcome was defined as BMI \geq 40, then physical (OR=1.34, 95% CI: 1.08-1.66), sexual (OR=1.81, 95% CI: 1.26-2.60), and any maltreatment (OR=1.25, 95% CI: 1.04-1.50) were all significantly associated with extreme obesity.

Based on the unadjusted results, an adjusted model was created for the associations between maltreatment and adulthood obesity as measured by $BMI \geq 40$. After adjusting for sex, race/ethnicity, and maternal education, physical maltreatment was significantly associated with extreme obesity (OR=1.37, 95% CI: 1.11-1.70). Sexual maltreatment was also significantly associated with extreme obesity (OR=1.72, 95% CI: 1.18-2.51), as was any maltreatment (OR=1.28, 95% CI: 1.06-1.53). Interaction terms for sex by physical and sexual maltreatment were not statistically significant at the 0.05 alpha level ($p = .77$ and $.29$, respectively). However, the association between neglect and extreme obesity was stronger for males (AOR=1.47, 95% CI: 1.05-2.07) than for females (AOR=0.95, 95% CI: 0.70-1.30), after adjusting for confounders (interaction term: $p = .12$; see Table 6).

3.3.3. Mediation Analyses

Based on the results of the descriptive analyses and regression analyses, the outcome of $BMI \geq 40$ was selected for the mediation analyses. As shown in Table 3, the indirect effect of mediation (ab) of adolescent depressive symptoms on the relationship between physical maltreatment and $BMI \geq 40$ was 0.22 (95% CI: 0.11-0.34). The indirect effect of mediation of adolescent body mass index was 0.05 (95% CI: 0.03-0.08). The effect of both mediating variables together in the multiple mediator model was 0.23 (95% CI: 0.02-0.43). Adjusting for adolescent depressive symptoms and adolescent BMI in the logistic regression model caused the odds ratio to lose statistical significance, decreasing from 1.34 (95% CI: 1.08-1.66) to 1.18 (95% CI: 0.92-1.52).

The indirect effect of mediation of adolescent depressive symptoms on the relationship between sexual maltreatment and BMI \geq 40 was 0.29 (95% CI: 0.12-0.47). The indirect effect of mediation of adolescent body mass index was 0.07 (95% CI: 0.02-0.12). The effect of both mediating variables together in the multiple mediator model was 0.30 (95% CI: 0.02-0.58). Adjusting for adolescent depressive symptoms and BMI in the logistic regression model did not cause a large change in the odds ratio.

Regarding the variable of any maltreatment, the indirect effect of mediation of adolescent depressive symptoms was 0.26 (95% CI: 0.14-0.39), and the indirect effect of mediation of adolescent BMI was 0.05 (95% CI: 0.02-0.07). The effect of both mediating variables together in the multiple mediator model was 0.25 (95% CI: 0.03-0.47). Adjusting for adolescent depressive symptoms and BMI in the logistic regression model caused the odds ratio to lose statistical significance, decreasing from 1.25 (95% CI: 1.04-1.50) to 1.15 (95% CI: 0.91-1.45).

3.3.4. Self-rated Weight

The associations between childhood maltreatment and self-rated weight (very overweight compared to very underweight, slightly underweight, about right, or slightly overweight) are shown in Table 4. Physical maltreatment was significantly associated with self-rating oneself as very overweight (OR=1.23, 95% CI: 1.03-1.48; AOR=1.27, 95% CI: 1.06-1.52), as was any maltreatment (OR=1.21, 95% CI: 1.03-1.43; AOR=1.27, 95% CI: 1.08-1.50).

As shown in Table 5, the indirect effect of mediation of adolescent depressive symptoms on the relationship between physical maltreatment and self-rated overweight

was 0.19 (95% CI: 0.09-0.29). The indirect effect of mediation of adolescent BMI was 0.03 (95% CI: 0.02-0.05). In the multiple mediator model, the indirect effects of mediation of depressive symptoms and adolescent BMI together was 0.11 (95% CI: 0.01-0.20), and adjusting for both variables caused the direct effect estimate to decrease from 1.23 (95% CI: 1.03-1.48) to 1.11 (95% CI: 0.90-1.35) and lose significance.

Regarding the independent variable of any maltreatment, the indirect effects of mediation of both adolescent depressive symptoms ($ab=0.22$, 95% CI: 0.11-0.33) and BMI ($ab=0.03$, 95% CI: 0.02-0.05) were statistically significant. In the multiple mediator model, the indirect effects of mediation totaled 0.11 (95% CI: 0.02-0.21). Adjusting for both variables caused the direct effect estimate to decrease from 1.21 (95% CI: 1.03-1.43) to 1.13 (95% CI: 0.93-1.36) and lose significance.

3.4. Discussion

The current study examined the relationship between multiple types of childhood maltreatment and adulthood obesity. Similar to previous studies, physical and sexual maltreatment were moderately associated with adulthood obesity (Danese & Tan, 2014; Midei & Matthews, 2011; Shin & Miller, 2012), and there was a stronger association for sexual maltreatment than for physical maltreatment, such as observed in the study by Keeshin and colleagues (2013). Therefore, experiencing at least one event of sexual maltreatment appears to be an especially traumatic event more so than physical maltreatment or neglect. It is apparent that sexual maltreatment is a multifaceted problem with complex dynamics, resulting in long term psychological consequences (including

emotional reactions, depression, anxiety, shame, and guilt), as well as problems with interpersonal relationships, and problems with sexual adjustment (Barnett, 2005).

These associations were true for both males and females; although stratum specific estimates appeared different in magnitude as hypothesized, effect modification by sex was not statistically significant for physical or sexual maltreatment. The association of neglect and extreme obesity was stronger for males than females, and the interaction was marginally significant. However, we found that overall, neglect was not strongly associated with adult obesity, in contrast with a previous study that used latent curve modeling of BMI/obesity in adolescence rather than adulthood (Shin & Miller, 2012). In post hoc analyses, childhood maltreatment was not found to be significantly associated with underweight ($BMI \leq 18.5 \text{ kg/m}^2$), possibly in part due to the small number of participants who met criteria for underweight at Wave IV (results not shown).

Interestingly, when we further categorized obesity into obese ($30\text{-}40 \text{ kg/m}^2$) and extremely obese ($\geq 40 \text{ kg/m}^2$), more independent variables were associated with the extreme obesity outcome. Using the CDC's definition of obesity, $BMI \geq 30 \text{ kg/m}^2$, resulted in only one significant association, between sexual maltreatment and obesity; however, when the definition was changed to $BMI \geq 40 \text{ kg/m}^2$, then both physical and sexual maltreatment were significantly associated with obesity, as well as the "any maltreatment" variable which included physical maltreatment, sexual maltreatment, and neglect. The effect estimates for sexual maltreatment were also higher for the more stringent BMI cutoff. Therefore, childhood maltreatment was more strongly associated with extreme obesity in adulthood than moderate obesity; one possible factor contributing to this effect could be the high prevalence of obesity in the sample and in the U.S. A BMI

of 30 might be considered more “normal” today, and may not symbolize a true mental disorder or pathology as in the past. This is important to consider in future research and patient counseling, as a patient with BMI of 30 and a patient with BMI of 40 may have different contributing factors and treatment needs.

Sexual maltreatment in childhood was associated with 72% higher odds of having a body mass index over 40 kg/m^2 in adulthood, after adjusting for demographic variables. Physical maltreatment was associated with 37% higher odds of $\text{BMI} \geq 40$, and experiencing any maltreatment in childhood including sexual maltreatment, physical maltreatment, or neglect, was associated with 28% higher odds of having a $\text{BMI} \geq 40$ in adulthood. These results support previous literature which has reported that childhood maltreatment is associated with adulthood obesity and central adiposity (Fang & Corso, 2007). Sex did not have a moderating effect as hypothesized and as seen in some previous literature (Schneiderman, et al., 2012).

The physical maltreatment and any maltreatment variables were also significantly associated with self-rated obesity, but surprisingly, sexual maltreatment was not. Descriptive analyses showed that there was a discrepancy between obesity defined by BMI and self-rated obesity for some participants; only 66% of those with a self-reported $\text{BMI} \geq 40$ responded that they were “very overweight.” Again, this is almost certainly due to the increased prevalence of obesity in the U.S. today; when more of one’s peers and family members also have a BMI in the obese range, then the state of obesity becomes normalized and one’s conception of what constitutes obesity is altered. Interestingly however, this discrepancy was even larger in those reporting sexual maltreatment; only 56.4% of those with $\text{BMI} \geq 40$ responded that they were “very overweight.” This finding

may indicate that individuals who have experienced sexual maltreatment are not only more likely to become obese later in life, but also more likely to have distorted views of their own weight. Hussey, Chang, & Kotch (2006) reported an association between sexual maltreatment and later overweight (defined as >85th percentile for BMI using interviewer measurements for height and weight; OR=1.35, $p<.05$; AOR=1.25, $p>.05$), as well as self-rating one's health as "fair" or "poor" (OR=2.06, $p<.001$; AOR=1.65, $p<.05$). However, Hussey et al.'s study did not examine self-rating of weight. It is apparent that experiencing maltreatment as a child has long lasting effects on not only one's body composition, but also the mental perception of one's body composition.

The most stringent criteria for obesity, BMI over 40 kg/m², were selected for mediation analyses based on the results of the logistic regression models, and also because these criteria likely represent the individuals with obesity of a more pathological nature (e.g., overeating to satisfy an emotional need). Testing the mediation effect of two adolescent variables, depressive symptoms and body mass index, revealed that both variables did have a statistically significant mediational effect on the associations of physical maltreatment, sexual maltreatment, and any maltreatment with extreme obesity. Depressive symptoms and BMI at Wave I were responsible for a large proportion of the association between maltreatment and obesity for all three maltreatment variables (results not shown). Adjusting for the depressive symptoms and adolescent BMI variables in the logistic regression analyses did not cause a large change in the effect estimate for sexual maltreatment, but did cause the effect estimates for physical maltreatment and any maltreatment to lose statistical significance. Similarly, adolescent depressive symptoms and BMI had significant indirect effects of mediation on the relationship between

physical maltreatment and any maltreatment with self-rated obesity. Adolescent BMI especially had a large mediational effect for both obesity variables; although the effects calculated by the formula ab appeared smaller than those of depressive symptoms due to the continuous nature of the variable, adjusting for BMI caused large decreases in the effect estimates. Therefore, it appears that these adolescent characteristics are indeed mechanisms on the causal pathway between experiencing maltreatment in childhood and extreme obesity in adulthood. To our knowledge, there is very little previous research using these variables, and this may be the first study to report some of these mediational associations. A recent systematic review and meta-analysis reported that adulthood depression was likely to be a significant mediator in this association, but did not report on any studies that tested adolescent depression (Danese & Tan, 2014).

The fact that adolescent depressive symptoms and BMI were significant mediators in the relationship between childhood maltreatment and adulthood obesity shows that the effects of maltreatment have begun to manifest by adolescence. Some victims of maltreatment have begun to display symptoms of depression and maladaptive coping behaviors such as overeating. In addition, it has been suggested that stressful adverse events (such as maltreatment) can increase inflammation and stress hormones in the body, increasing the propensity to gain weight (Coelho, et al., 2014). In the case of sexual maltreatment victims, overeating may serve as a way to decrease attractiveness and thus prevent unwanted sexual interest from others, which is sometimes viewed as an adaptive function of obesity (Gustafson & Sarwer, 2004). Thus, childhood maltreatment sets mental and behavioral patterns into motion for the rest of the individual's life that lead to overeating and overweight. Adolescence provides an ideal opportunity for

professionals such as high school guidance counselors to identify individuals who are displaying some of these symptoms and behaviors, to identify potential maltreatment victims and recommend interventions to increase social and coping skills, before the individual reaches adulthood and negative patterns become more permanent.

The limitations of this study mostly pertain to the Add Health study design. The retrospective measurement of childhood maltreatment may be vulnerable to some measurement/recall bias, if participants inaccurately reported their past experiences due to misremembering or embarrassment. Another potential limitation is the self-reported body mass index variable. BMI has been previously validated as a measure of body fatness. This study used self-reported height and weight to calculate BMI, which is less accurate than if these measurements were made by a clinician; however, self-reported BMI has been previously shown to be a fairly accurate indicator of overweight and obesity (Sherry, Jefferds, & Grummer-Strawn, 2007). Finally, there were a number of participants whose data was excluded due to missing data for at least one maltreatment variables, likely due to negative feelings about experienced maltreatment; sensitivity analyses showed that these participants were slightly more likely to be obese than participants without missing maltreatment data (39% vs. 37%). Therefore, the effect estimates may have been slightly underestimated if our assumptions are correct that the individuals with missing data were more likely to have experienced maltreatment and be obese in adulthood.

Despite the above limitations, this study also has a number of strengths. The Add Health dataset is a large, nationally representative dataset with a large sample size and a longitudinal design following participants from adolescence to adulthood. The analyses

were weighted using the sample weights provided, meaning that the conclusions drawn from this study have implications for American adolescents and adults. Strengths of this specific study include the use of the childhood neglect variable, which is rarely included in studies of childhood maltreatment. Obesity was calculated in three different ways, ≥ 30 , ≥ 35 , and ≥ 40 kg/m², as well as measured with a self-rated weight question, to more thoroughly assess both the participant's weight and mental concept of their own weight status. Additionally, we found a statistically significant mediational effect of adolescent depressive symptoms in the association between child maltreatment and obesity (both objective and subjective measures), which to our knowledge has not been reported in previous literature (Danese & Tan, 2014; Midei & Matthews, 2011). Lastly, the use of MacKinnon's method of testing mediation rather than the method described by Baron and Kenny is a strength, because it allows statistical testing of mediation, and it can be used for single and multiple mediator models, which are distinct advantages.

3.5. Conclusions

This study adds to the existing literature by showing indirect effects of mediation of adolescent depressive symptoms and BMI in the relationship between childhood maltreatment (including physical maltreatment, sexual maltreatment, and neglect) and adulthood obesity. A relationship was shown using self-rated weight status as well as multiple thresholds of body mass index to measure the outcome of obesity. Measuring obesity in different ways led to different results and conclusions, and we suggest that future research take this into consideration when determining measurement of endpoints. This study lends support to the hypothesis that adverse events such as maltreatment that

occur in childhood can have long lasting effects on both mental and physical health in adolescence and adulthood. Future research may investigate potential interventions based on the adolescent characteristics of depressive symptoms and BMI, that may lessen the risk of obesity and related health problems for maltreatment victims.

3.6. Tables and Figures

Figure 1. Conceptual Framework

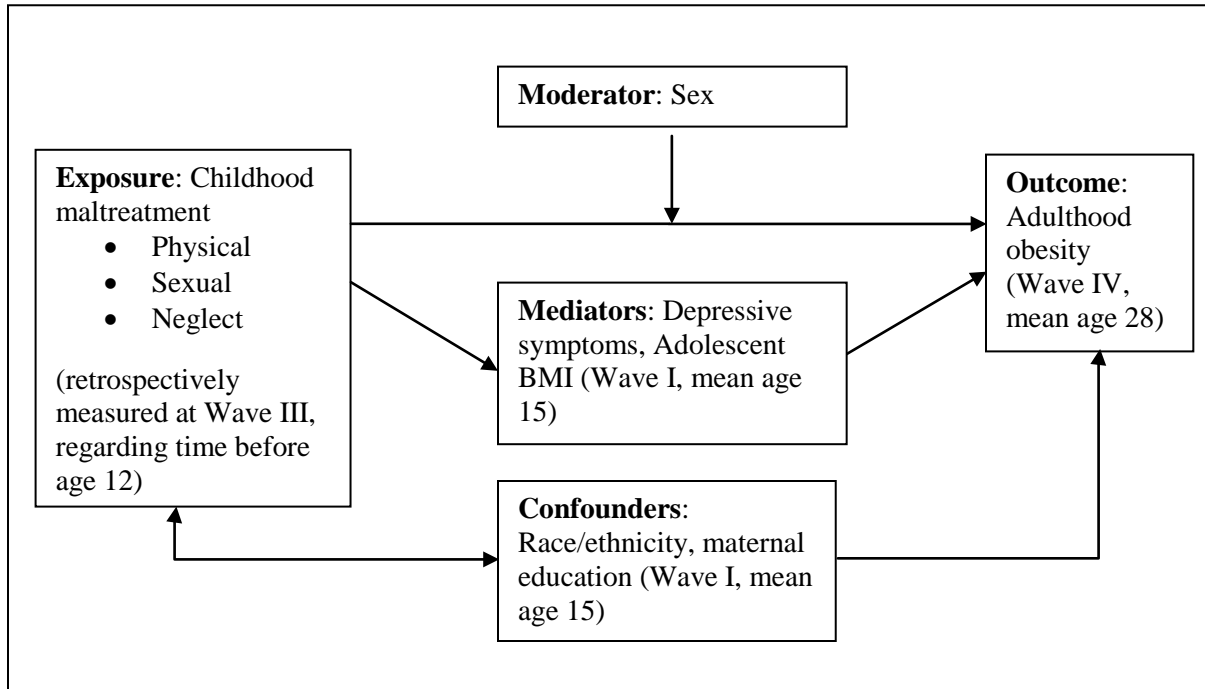


Table 1. Descriptive characteristics of sample (unweighted numbers, weighted percentages).

	Total (n=10,894)	Not Meeting Criteria for Extreme Obesity ($<40 \text{ kg/m}^2$; n=9,874)	Met Criteria for Extreme Obesity ($\geq 40 \text{ kg/m}^2$; n=1,020)	p value
Sex (n, weighted %)				<.0001
Male	4,832 (47.8)	4,490 (48.8)	342 (38.1)	
Female	6,062 (52.2)	5,384 (51.2)	678 (61.9)	
Race/ethnicity				<.0001
White	6,169 (69.4)	5,703 (70.1)	466 (61.7)	
African American	2,267 (14.9)	1,948 (14.0)	319 (23.1)	
Hispanic	1,664 (11.4)	1,488 (11.4)	176 (11.6)	
Asian	673 (3.3)	634 (3.5)	39 (1.5)	
American Indian/Native American	92 (0.8)	72 (0.6)	20 (1.9)	
Missing	29 (0.3)	29 (0.3)	0 (0)	
Maternal education				<.0001
Less than HS	1,438 (13.2)	1,245 (12.7)	193 (18.8)	
HS or GED	2,837 (28.8)	2,558 (28.4)	279 (32.5)	
Some college	2,774 (25.3)	2,542 (25.8)	232 (20.6)	
College or greater	2,380 (20.5)	2,209 (21.0)	171 (15.3)	
Missing	1,465 (12.1)	1,320 (12.1)	145 (12.8)	
Child maltreatment				
Physical	3,207 (28.3)	2,863 (27.8)	344 (34.0)	.0072
Sexual	535 (4.8)	459 (4.5)	76 (7.8)	.0012
Neglect	2,148 (19.5)	1,923 (19.3)	225 (21.5)	.2091
Any maltreatment	4,210 (37.9)	3,774 (37.5)	436 (42.7)	.0202
Depressive Symptoms				<.0001
Meets cutoff	859 (7.4)	737 (7.1)	122 (11.0)	
Does not meet cutoff	10,035 (92.6)	9,137 (92.9)	898 (89.0)	
Adolescent BMI (mean, SD)	22.6 (4.5)	21.9 (3.6)	29.8 (5.5)	<.0001
Self-rated weight				<.0001
Very overweight	1,565 (13.7)	880 (8.4)	685 (66.0)	
Slightly overweight, normal weight, slightly underweight, or very underweight	9,326 (86.3)	8,991 (91.6)	335 (34.0)	

*Between group differences were tested by PROC SURVEYMEANS for age and adolescent BMI, and PROC SURVEYFREQ (Chi Square test) for all other variables.

Table 2. Unadjusted and adjusted associations (odds ratios and 95% confidence intervals) between types of childhood maltreatment and adult obesity as measured by three BMI cutoffs (BMI ≥ 30 , ≥ 35 , or ≥ 40 kg/m²).

<i>Childhood maltreatment</i>	<i>Obese (BMI ≥ 30 kg/m²)</i>	<i>Unadjusted</i>		<i>Adjusted*</i>
		<i>Moderately Obese (BMI ≥ 35 kg/m²)</i>	<i>Extremely Obese (BMI ≥ 40 kg/m²)</i>	<i>Extremely Obese (BMI ≥ 40 kg/m²)</i>
Physical maltreatment	1.07 (0.92-1.25)	1.20 (1.01-1.43)	1.34 (1.08-1.66)	1.37 (1.11-1.70)
Sexual maltreatment	1.34 (1.05-1.72)	1.40 (1.03-1.90)	1.81 (1.26-2.60)	1.72 (1.18-2.51)
Neglect	1.13 (0.98-1.30)	1.06 (0.92-1.23)	1.15 (0.93-1.42)	1.17 (0.94-1.44)
Any maltreatment	1.09 (0.95-1.25)	1.12 (0.96-1.30)	1.25 (1.04-1.50)	1.28 (1.06-1.53)

*Models were adjusted for sex, race/ethnicity, and maternal education.

Table 3. Direct effect estimates of Indirect effects of the association between childhood maltreatment and adult extreme obesity (≥ 40 kg/m²), and indirect effects of mediation of adolescent depressive symptoms and adolescent BMI.

		<i>Exposure Variable</i>		
		<i>Physical maltreatment</i>	<i>Sexual maltreatment</i>	<i>Any maltreatment</i>
<i>Indirect Effects of Mediation</i>				
	Adolescent depressive symptoms	0.22 (0.11-0.34)	0.29 (0.12-0.47)	0.26 (0.14-0.39)
	Adolescent BMI	0.05 (0.03-0.08)	0.07 (0.02-0.12)	0.05 (0.02-0.07)
	Adolescent depressive symptoms and BMI	0.23 (0.02-0.43)	0.30 (0.02-0.58)	0.25 (0.03-0.47)
<i>Direct Effects</i>				
	Unadjusted odds ratio	1.34 (1.08-1.66)	1.81 (1.26-2.60)	1.25 (1.04-1.50)
	AOR (adjusting for adolescent depressive symptoms)	1.32 (1.06-1.63)	1.77 (1.23-2.55)	1.22 (1.01-1.47)
	AOR (adjusting for adolescent BMI)	1.19 (0.93-1.53)	1.92 (1.15-3.20)	1.17 (0.93-1.47)
	AOR (adjusting for adolescent depressive symptoms and BMI)	1.18 (0.92-1.52)	1.91 (1.15-3.19)	1.15 (0.91-1.45)
	AOR (adjusting for adolescent depressive symptoms, BMI, and confounders)	1.25 (0.97-1.60)	2.02 (1.21-3.37)	1.23 (0.98-1.55)

Table 4. Associations between childhood maltreatment and adulthood self-rated weight status (very overweight compared to very underweight, slightly underweight, about right, or slightly overweight).

<i>Childhood maltreatment</i>	<i>Unadjusted OR</i>	<i>Adjusted OR*</i>
Physical maltreatment	1.23 (1.03-1.48)	1.27 (1.06-1.52)
Sexual maltreatment	1.31 (0.94-1.82)	1.30 (0.93-1.82)
Neglect	1.02 (0.87-1.20)	1.12 (0.94-1.32)
Any maltreatment	1.21 (1.03-1.43)	1.27 (1.08-1.50)

*Models were adjusted for sex, race/ethnicity, and maternal education.

Table 5. Direct effect estimates of the association between childhood maltreatment and self-rated adult obesity, and indirect effects of mediation of adolescent depressive symptoms and adolescent BMI.

		<i>Exposure Variable</i>	
		<i>Physical maltreatment</i>	<i>Any maltreatment</i>
<i>Indirect Effects of Mediation</i>			
	Adolescent depressive symptoms	0.19 (0.09-0.29)	0.22 (0.11-0.33)
	Adolescent BMI	0.03 (0.02-0.05)	0.03 (0.02-0.05)
	Adolescent depressive symptoms and BMI	0.11 (0.01-0.20)	0.11 (0.02-0.21)
<i>Direct Effects</i>			
	Unadjusted odds ratio	1.23 (1.03-1.48)	1.21 (1.03-1.43)
	AOR (adjusting for adolescent depressive symptoms)	1.22 (1.02-1.46)	1.20 (1.02-1.42)
	AOR (adjusting for adolescent BMI)	1.11 (0.91-1.35)	1.13 (0.93-1.37)
	AOR (adjusting for adolescent depressive symptoms and BMI)	1.11 (0.90-1.35)	1.13 (0.93-1.36)
	AOR (adjusting for adolescent depressive symptoms, BMI, and confounders)	1.16 (0.96-1.40)	1.21 (1.01-1.44)

Table 6. Effect modification by sex.

	BMI>40		Self-Rated Obesity	
	Males	Females	Males	Females
Childhood maltreatment				
Physical	1.33 (0.91-1.96)	1.41 (1.11-1.79)	1.34 (0.97-1.87)	1.24 (1.02-1.51)
Sexual	2.29 (1.26-4.15)	1.46 (0.97-2.18)	1.08 (0.56-2.08)	1.45 (0.98-2.16)
Neglect	1.47 (1.05-2.07)	0.95 (0.70-1.30)	1.21 (0.87-1.68)	1.07 (0.87-1.31)
Any maltreatment	1.32 (0.94-1.84)	1.26 (1.02-1.56)	1.29 (0.97-1.72)	1.26 (1.05-1.52)

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Chapter 4 (Paper 2): The Pathway from ADHD Symptoms to Alcohol Dependence, Mediated by Adolescent Depressive Symptoms and Delinquent Behavior

Introduction

Childhood Attention Deficit Hyperactivity Disorder (ADHD) has been linked to later alcohol use disorder (AUD) especially dependence; however, the mechanisms of this relationship have not been well studied. This study examined the association between childhood ADHD symptoms and adulthood alcohol dependence, and the mediating effects of adolescent depressive symptoms, delinquency, alcohol consumption, and friends' alcohol consumption.

Methods

Weighted logistic regression analysis was conducted to examine the association between self-reported childhood ADHD symptoms and alcohol dependence in 11,038 participants in the National Longitudinal Study of Adolescent to Adult Health. Mediation by adolescent depressive symptoms, delinquency, alcohol consumption, and friends' alcohol consumption at Wave I was tested using MacKinnon's method.

Results

Adolescent delinquency was a statistically significant mediator in the pathway between ADHD symptoms and alcohol dependence, accounting for 9.7% of the total effect. The indirect effects of mediation of adolescent alcohol consumption and friends'

alcohol consumption were also statistically significant, accounting for 17.3% and 10.9% of the total effect, respectively. Adolescent depressive symptoms were not a significant mediator. In the multiple mediator model, delinquency and alcohol consumption together accounted for 19.0% of the total effect, and caused the odds ratio of the main association to decrease from 1.97 (95% CI: 1.55-2.50) to 1.72 (95% CI: 1.34-2.20).

Conclusions

A child with ADHD symptoms may develop maladaptive coping methods such as delinquent behavior (including drinking alcohol) in adolescence, increasing risk for later alcohol dependence. Children with ADHD symptoms, especially those showing signs of delinquent behavior, may need extra support to reduce the future risk of alcohol dependence.

Keywords: ADHD, Alcohol use disorder, Alcohol dependence, Delinquency, Depression, Adolescent health

4.1. Introduction

Previous research has shown an association between Attention Deficit Hyperactivity Disorder (ADHD) in childhood and alcohol use disorder (AUD) in adulthood. A meta-analysis of ten prospective cohort studies reported 35% higher risk of AUD (95% CI: 11-64%) after the age of 18 for those who met criteria for ADHD in childhood (Charach et al., 2011). Individuals with ADHD may be more likely to experience depressive symptoms as well as early alcohol use, which may be a precursor to AUD. However, there is a paucity of literature that closely examines potential mechanisms in this relationship.

ADHD symptoms such as attentional difficulties and hyperactivity/impulsivity affect performance and behavior at school and at home (American Psychiatric Association, 2000), causing the child to experience adverse events such as poor grades and negative attention from parents, teachers, and peers. A child with ADHD symptoms may have trouble making friends due to socially inappropriate hyperactive behavior, and decreased ability to follow social rules. Early childhood adversity such as troubled relationships with parents, teachers, and peers can disrupt the development of brain structure and function, and lead to maladaptive methods of coping with future stress and adversity, such as alcohol abuse (Dube et al., 2002; Shonkoff et al., 2012). By adolescence, associating with delinquent peers and performing delinquent behavior such as drinking alcohol may be observed. Qualitative research suggests that one reason that adolescents with ADHD may associate with peers who use alcohol, and begin to use alcohol, is to obtain a sense of belongingness with peers (Nehlin et al, 2015). In addition, adolescents with ADHD symptoms may find school frustrating and even pointless, which

decreases motivation to behave well and avoid trouble. However, these delinquent adolescent behaviors can have important negative consequences into adulthood. Studies have shown that adolescent delinquency, especially earlier alcohol consumption, is associated with higher risk of later AUD (Harford & Muthen, 2000; White & Gorman, 2000). Previous research has suggested that adolescent drinking may mediate the relationship between chronic stress in childhood and alcohol dependence in adulthood (Enoch, 2011). Thus, adolescent delinquency and alcohol consumption are likely mediators in the relationship between ADHD symptoms and AUD, as well as peers' alcohol consumption.

Similarly, a child's poor performance in school and possible bullying by peers due to ADHD symptoms may lead to negative feelings, low self-esteem, and other symptoms of depression by adolescence (Taurines et al., 2010). These depressive symptoms in adolescence may be associated with the adoption of maladaptive coping behaviors such as drinking alcohol, to cope with negative feelings (Thornton et al., 2012). Depression and AUD have a very high co-morbidity; a meta-analysis reported that after adjusting for sociodemographic and other confounders, an association between depression and AUD remained, with pooled adjusted odds ratios around 2.00 (Boden & Fergusson, 2011). Therefore, adolescent depressive symptoms are another possible mediator in the relationship between ADHD symptoms and AUD. However, there has not been much research to statistically test the effects of mediation of depressive symptoms or adolescent delinquency.

In the current study, adolescent delinquency, depressive symptoms, alcohol consumption and friends' alcohol consumption were tested as potential mediating

variables in the association between childhood ADHD symptoms and adulthood alcohol dependence.

4.2. Methods

4.2.1. Dataset

This study was a secondary data analysis of Waves I, III, and IV of the National Longitudinal Study of Adolescent to Adult Health (UNC Carolina Population Center, 2011). The Add Health study used a multistage stratified cluster design and included four waves of data collection from adolescence to adulthood. Data were collected using in-person interview, as well as computer-assisted self-interview for sensitive questions. In total, 12,288 participants had data and sample weights for Waves I (mean age 15.4), III (mean age 21.8), and IV (mean age 28.3). Cases were excluded from analyses if they were missing data for the exposure variable, mediating, or outcome variable, leaving an analytic sample size of 11,038.

4.2.2. Measures

4.2.2.1. Dependent variable: Adulthood alcohol dependence

For this study, the outcome was defined as lifetime alcohol dependence, which is a more clinically meaningful construct compared to alcohol abuse, with stricter criteria for physiological symptoms. Questions about use, frequency, amount, and consequences of alcohol consumption were used to construct a variable measuring lifetime alcohol dependence (harmful use plus physical dependency symptoms or being unable to quit

drinking) at Wave IV. Answering positively to three of the dependence symptoms would classify the participant as positive for alcohol dependence (AUD). These questions were based on DSM-IV criteria, including increasing tolerance to alcohol, withdrawal symptoms after stopping use, using more alcohol than intended, unsuccessful attempts to quit, spending a lot of time obtaining, using, and recovering from alcohol, giving up activities because of alcohol use, and continued use after knowledge of recurrent physical or psychological sequelae (American Psychiatric Association, 2000).

4.2.2.2. Independent variable: Childhood ADHD symptoms

Childhood ADHD symptoms were assessed retrospectively at Wave III with 17 questions about the respondent's behavior between 5 and 12 years of age, dichotomized into two domains, hyperactivity/impulsivity (HI) and inattention (IN). Wording and choice of questions reflect DSM-IV criteria for clinician diagnosis of ADHD, with two exceptions. The DSM-IV impulsivity symptom of "Often interrupts or intrudes on others (e.g., butts into conversations or games)" was not included on the Add Health questionnaire. "You were spiteful or vindictive" was asked instead, which is not a DSM-IV symptom and therefore was excluded from current analyses, resulting in a total of 8 HI symptoms and 9 IN symptoms. Each question had the following response options: never or rarely, sometimes, often, or very often. Following the precedent set by Kollins et al., 2005, respondents were coded as reporting a symptom present if they answered often or very often. A cutoff of six symptoms was used for each domain, consistent with DSM-IV criteria. Respondents were classified into two ADHD symptom groups: (1) met criteria for one or both domains, and (2) did not meet criteria for either domain.

4.2.2.3. Mediators: Adolescent Characteristics

Depressive Symptoms. Depressive symptoms were measured at Wave I during adolescence, using the “Feelings Scale” of the Add Health dataset, which is modeled closely after the widely used Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977). The Feelings Scale includes 19 questions about feelings in the past week. Each question was coded on a scale from 0 to 3. Totals were summed over the 19 questions, and possible score totals ranged from 0 to 57. Cutoff scores of 22 for males and 24 for females were used to classify respondents as being at risk for depression during adolescence, based on cutoff scores used in previous literature (Roberts et al., 1991). The total score (0-57) and the dichotomized variable using the depressive symptom cutoff were tested separately in mediation analyses.

Delinquency. The Add Health dataset contains a scale to measure delinquency in the last 12 months at the time of Wave I. The scale included questions that reflected behaviors such as property crime, violent crime, status offenses, drug sales, and disturbing the peace. Each question was coded as follows: never, or ≥ 1 time. The 15 delinquency variables were summed into a total delinquency score (0-15). These questions have been used previously to measure adolescent delinquency at Wave I (Aalsma et al., 2010, Armour & Haynie, 2007).

Alcohol consumption and friends’ alcohol consumption. Participants were asked the following question at Wave I: “Do you ever drink beer, wine, or liquor when you are not with your parents or other adults in your family?” This variable was coded dichotomously (yes or no). The second question was “Of your 3 best friends, how many

drink alcohol at least once a month?” This variable was coded as follows: zero, one, two, or three friends.

4.2.2.4. Confounders

Participant sex, race/ethnicity, physical maltreatment or neglect, and parental AUD were used as confounders in analyses. Self-reported race/ethnicity of the participant was coded as follows: non-Hispanic White, non-Hispanic Black, Hispanic, Asian, or Other. Maltreatment experience (physical maltreatment or neglect) before entering sixth grade was retrospectively assessed at Wave III. Participants who reported at least one instance of physical maltreatment, at least one instance of physical neglect, or more than five instances of supervisory neglect, were coded as experiencing childhood maltreatment or neglect, which is consistent with previous Add Health research (Fang & Corso, 2007). Parental AUD was coded as having at least one biological parent with AUD, as reported by a parent at Wave I.

4.2.3 Statistical analysis

Descriptive characteristics are shown in Table 1. Chi square tests were used to test for differences between subjects with or without alcohol dependence at Wave IV, for most variables. For total delinquency score, regression was used to test for between group differences. PROC SURVEYLOGISTIC (SAS software version 9.3; Cary, NC) was used to conduct weighted logistic regression analysis to examine the association between ADHD symptoms and alcohol dependence. Sample weights were applied to account for the complex sample design.

To test for the mediating effect of adolescent depressive symptoms, delinquency, alcohol consumption, and friends' alcohol consumption, the method described in MacKinnon (2008) was used. This method improves upon the classical method described in Baron & Kenny (1986) because mediation effects can be quantified, rather than just testing whether mediation is present. The following three models were used, where Y is the outcome (alcohol dependence), X is the exposure (ADHD symptoms), and M is the mediator (depressive symptoms, delinquency, adolescent alcohol consumption, or friends' alcohol consumption):

$$1) Y = i_1 + cX + e_1$$

$$2) Y = i_2 + c'X + bM + e_2$$

$$3) M = i_3 + aX + e_3$$

These three equations describe three parts of the theoretical description of mediation: 1) the exposure is associated with the outcome, 2) the mediator is associated with the outcome while controlling for the exposure, and 3) the exposure is associated with the mediator.

Mediation analysis therefore included three logistic regression analyses to test each mediator ("single mediator models"). The indirect effect of mediation was calculated with the equation ab , and the proportion of total effect mediated was calculated with the equation ab/c (MacKinnon, 2008). This method is relatively new but has been used in recent public health research (De Cocker et al., 2015). Another final mediation analysis was conducted with all statistically significant mediator variables ("multiple mediator model"), using the following models:

$$1) Y = i_1 + cX + e_1$$

$$2) Y = i_2 + c'x + b_1M_1 + b_2M_2 + e_2$$

$$3) M_1 = i_3 + a_1x + e_3$$

$$4) M_2 = i_4 + a_2x + e_4$$

In the formulas above, a_1 is the parameter relating the independent variable to the first mediating variable, a_2 is the parameter relating the independent variable to the second mediating variable, b_1 and b_2 are the parameters relating the first and second mediators to the dependent variable adjusted for the effects of the independent variable, c represents the relation between the independent variable to the dependent variable, and c' represents the relation between the independent variable to the dependent variable adjusted for the effects of the mediators (MacKinnon, 2008, pages 49-50). The indirect effect of mediation was calculated by the equation $a_1b_1+a_2b_2$, and the proportion of total effect mediated calculated by the equation $(a_1b_1+a_2b_2)/c$.

Finally, we conducted weighted logistic regression models including the mediators, in order to observe the effect of adjusting for the mediators on the effect estimates. A fully adjusted model included adjustment for confounders.

4.3. Results

4.3.1 Descriptive statistics

Regarding the outcome of meeting criteria for alcohol use disorder (alcohol dependence symptoms), 14.5% of the sample met criteria for alcohol dependence at Wave IV (see Table 1). This is comparable to previous research which reported that about 13% of adults had experienced alcohol dependence in their lifetime (Hasin et al., 2007). Regarding ADHD symptoms, 8.2% of the sample met criteria for one or both domain cutoffs. Those who met alcohol dependence criteria were more likely to meet criteria for at least one ADHD symptom domain in childhood than those who did not (13.5% vs. 7.3%; $p < .0001$). The differences in proportion of those who met the cutoff for depressive symptoms by alcohol dependence status were not statistically significant (9.2% vs. 7.1%, $p = .0506$). Those who met alcohol dependence criteria had a mean adolescent delinquency total score of 3.89, meaning that they endorsed an average of almost four delinquency questions, compared to an average of 2.53 delinquency questions endorsed by those who did not meet alcohol dependence criteria ($p < .0001$). Adolescent drinking when not with parents or family was reported by 41.0% of participants; the difference in proportion by alcohol dependence status was statistically significant (53.8% vs. 38.8%; $p < .0001$). Those who met alcohol dependence criteria were also more likely to report that at least one of their best friends drank alcohol at least once a month (65.7% vs. 52.4%; $p < .0001$).

4.3.2 Single Mediator Models

Adolescent depressive symptoms did not have a statistically significant mediating effect on the relationship between ADHD symptoms and alcohol dependence (see Table 2). The dichotomous depressive symptom cutoff variable was found to mediate 6.3% of

the total effect but the effect was not statistically significant ($ab=0.02$, 95% CI: -0.02-0.06).

The adolescent delinquency scale total score was found to significantly mediate the relationship between ADHD symptoms and alcohol dependence ($ab=0.04$, 95% CI: 0.03-0.04). The proportion of the total effect mediated by delinquency was 9.7%.

Adjusting for delinquency in the logistic regression model caused the unadjusted odds ratio for those who met criteria for one or both ADHD domains to decrease from 1.97 (95% CI: 1.55-2.50) to 1.74 (95% CI: 1.36-2.21; see Table 3).

The indirect effect of mediation was statistically significant for both drinking alcohol in adolescence ($ab=0.06$, 95% CI: 0.04-0.09) and number of three best friends who drink alcohol ($ab=0.04$, 95% CI: 0.02-0.06). These variables mediated 17.3% and 10.9% of the total effect, respectively.

4.3.3 Multiple Mediator Model

Adolescent delinquency and adolescent alcohol consumption were selected as potential mediators in the multiple mediator model based on the results of the single mediator models (friends' alcohol consumption was not included due to multicollinearity with adolescent alcohol consumption). In the multiple mediator model, delinquency and alcohol consumption were statistically significant, together accounting for 19.0% of the total effect ($ab=0.07$, 95% CI: 0.02-0.11; see Table 4). Adjusting for both variables resulted in an adjusted odds ratio of 1.72 (95% CI: 1.34-2.20). Adjusting for both variables and other confounders resulted in an adjusted odds ratio of 1.47 (95% CI: 1.15-1.89).

4.4. Discussion

In the current study, adolescent delinquency and alcohol consumption were found to mediate the relationship between childhood ADHD symptoms and adult alcohol dependence. Adjusting for both variables caused the odds ratio to decrease from 97% higher odds to 72% higher odds of later alcohol dependence for those who met criteria for one or both ADHD symptom domains, compared to those who did not meet criteria for either domain. These variables appeared to partially but not totally mediate the effect, as the odds ratio was still statistically significant after fully adjusting for these and other variables. Surprisingly, the indirect effect of mediation of adolescent depressive symptoms was not statistically significant. The depressive symptoms scale used was self-reported and may not have captured all clinical cases of depression, thus biasing the results toward the null. In post hoc analyses, different ways of coding depressive symptoms were tested, such as using a continuous variable or using three categories of depressive symptom score rather than two in order to capture “medium” risk or subclinical cases (e.g. scoring ≥ 22 for males or ≥ 24 for females to be considered high risk, 10-21 or 10-23 for medium risk, and ≤ 9 for low risk, as previously used by Beck, et al, 2009); however, the indirect effect of mediation of depressive symptoms was still not statistically significant.

Having more adolescent friends who drank alcohol also had a statistically significant indirect effect of mediation on the main association. This variable was not included in the multiple mediator model due to collinearity with adolescent drinking; for example, only 15.9% of adolescent drinkers reported that none of their three best friends

drank, compared to 63.0% of nondrinkers. This supports the hypothesis that association with drinking peers is associated with individual drinking. Although it is difficult to separate the effects of individual and peer alcohol consumption, we postulate that the individual with ADHD symptoms has social difficulties due to their symptoms, and seeks out other “misfit” peers who perform delinquent behaviors and underage drinking in order to find a sense of camaraderie and belongingness; it is this association with delinquent peers that increases the odds of adolescent alcohol consumption and later dependence. It is important to note that there are other possible direct and indirect effects at play as well, such as using alcohol’s depressant effects to calm hyperactive behavior; however, our results demonstrate that these adolescent characteristics are at least one feasible pathway from early chronic stress related to ADHD symptoms in childhood to alcohol dependence later in life.

Although previous research has documented a link between childhood ADHD and adulthood AUD (Charach et al., 2011), to our knowledge there has not been much research to test potential mediators of this relationship. In one study, data from 265 individuals in the Pittsburgh ADHD Longitudinal Study was used with structural equation modeling to assess the relationships between a clinical diagnosis of ADHD, Self-Reported Delinquency questionnaire score in adolescence (ages 14-17) and at age 20, and heavy alcohol use (frequency of binge drinking, and frequency of drunkenness) at age 20 (Molina, et al., 2014). The authors reported that childhood ADHD predicted more delinquency in adolescence which in turn predicted more delinquency at age 20; delinquency at age 20 was associated with more frequent heavy alcohol use at age 20. Thus there was a significant indirect effect from ADHD through delinquency to heavy

alcohol use ($p=.04$). However, there was no significant direct effect from ADHD to heavy alcohol use, which conflicts with other research. Heavy drinking in early adulthood is associated with adulthood AUD; however, not all heavy drinkers have a clinically diagnosable AUD. Therefore, these outcomes are meaningfully different from each other, and more research is still needed to investigate mechanisms in the relationship between ADHD symptoms and adulthood AUD, including adolescent delinquency as well as other potential mediators (such as ADHD medication or other treatments).

The relationship between childhood ADHD symptoms and adulthood AUD is complex, with many possible mechanisms at work. An individual who has symptoms of ADHD is likely to experience adversity due to his/her symptoms, including poor performance at school, low self-esteem, and negative attention from caregivers, even including possible maltreatment. These adverse events may cause stress and lead to maladaptive methods of coping in adolescence (Shonkoff et al., 2012). The adolescent may be more likely to perform delinquent behaviors such as skipping school (Molina, 2014) in order to avoid academic pressure, and begin to associate with other deviant peers, increasing exposure and access to early drinking. Individuals with ADHD may be more likely than others to seek a sense of belongingness with peers by participating in early alcohol use (Nehlin et al, 2015). In the present study, 51.6% of those with ADHD symptoms reported drinking alcohol, vs. 40% of adolescents without ADHD symptoms. Additionally, 64.5% of those with ADHD symptoms reported at least one best friend who drank alcohol, vs. 53.4% of those without ADHD symptoms. Thus, early ADHD symptoms may lead to a greater risk of association with delinquent peers and delinquent

behavior including alcohol use in adolescence, in turn leading to a greater risk of alcohol use disorder throughout adulthood.

The limitations of this study mostly pertain to the Add Health study design. The retrospective measurement of ADHD symptoms may be vulnerable to some measurement/recall bias, if participants inaccurately reported their past experiences due to misremembering or embarrassment. However, self-reported ADHD symptoms may be a more sensitive measure compared with clinical diagnosis, as it may catch more subclinical cases. In addition, self-reported alcohol dependence symptoms, alcohol consumption, friends' alcohol consumption, depressive symptoms, and delinquency may be vulnerable to bias, if participants were untruthful due to embarrassment or fear. We also note that there may be “diagnostic orphans” with some AUD or ADHD symptoms, who did not have enough symptoms to meet domain criteria; these individuals were classified in the same group with participants without any AUD or ADHD symptoms. Despite the above limitations, this study also has a number of strengths. The Add Health dataset is a large, nationally representative dataset with a large sample size and a longitudinal design following participants from adolescence to adulthood. The MacKinnon method of testing mediation offers advantages over the classic Baron & Kenny method, as described above.

4.5. Conclusions

This study adds to the existing literature by examining multiple potential mechanisms for the relationship between ADHD symptoms and later alcohol dependence, which have not been well studied in previous research. It has been established that early stressors can have long lasting ramifications on mental and physical

health throughout the lifespan. Therefore, the results of this study have implications for the consequences of stress early in life, such as that incurred by living with symptoms of a condition such as ADHD. Children with ADHD symptoms, especially those who display delinquent behavior, may need extra support, such as training in social/coping skills, to reduce the risk of developing maladaptive coping behaviors such as drinking alcohol. This study offers insight into possible trajectories of multiple negative health outcomes, and has strong implications for identifying and treating vulnerable children before and during adolescence. Future research may aim to further explore these relationships, including the effect of ADHD treatments and intervention possibilities for delinquent adolescents.

Conflict of Interest

The authors have no conflicts of interest to report.

4.6. Tables and Figures

Figure 1. Conceptual Framework

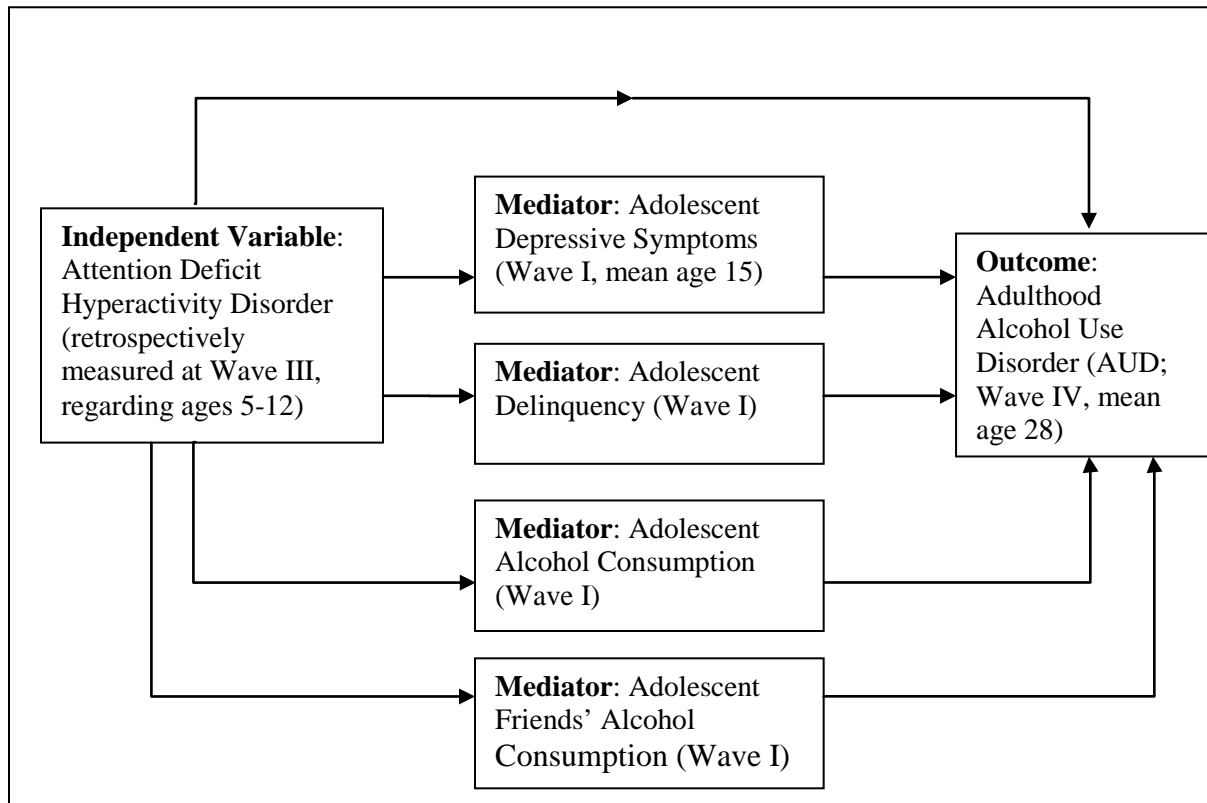


Table 1. Descriptive characteristics of sample by AUD status (unweighted numbers, weighted percentages).

	Total (n=11,038)	No alcohol use disorder (n=9,592; 85.5%)	Met criteria for alcohol use disorder (n=1,446; 14.5%)	p value
ADHD Symptoms				<.0001
Meets neither cutoff	10,207 (91.8)	8,946 (92.7)	1,261 (86.5)	
Meets either cutoff	831 (8.2)	646 (7.3)	185 (13.5)	
Depressive Symptoms				.0506
Does not meet cutoff	10,172 (92.6)	8,856 (92.9)	1,316 (90.8)	
Meets cutoff	866 (7.4)	736 (7.1)	130 (9.2)	
Delinquency Score				
Total score (Mean, SE)	2.75 (0.05)	2.53 (.05)	3.89 (.11)	<.0001
Adolescent alcohol consumption				<.0001
No	6,520 (59.0)	5,874 (61.2)	646 (46.1)	
Yes	4,513 (41.0)	3,714 (38.8)	799 (53.8)	
Missing	5 (0.0)	4 (0.0)	1 (0.1)	
Adolescent friends' alcohol consumption				<.0001
No friends	4,788 (43.7)	4,310 (45.5)	478 (33.6)	
One friend	2,347 (20.5)	2,004 (19.6)	343 (25.2)	
Two friends	1,614 (14.1)	1,397 (14.1)	217 (13.7)	
Three friends	2,106 (19.8)	1,710 (18.7)	396 (26.8)	
Missing	183 (1.9)	171 (2.1)	12 (0.7)	

*Between group differences were tested by PROC SURVEYREG for Delinquency Score, and PROC SURVEYFREQ

(Chi Square test) for all other variables.

Table 2. Results of single mediator models.

	Indirect effect of mediation (ab) and 95% CI	Proportion of total effect mediated
Depressive symptoms	0.02 (-0.02-0.06)	6.3%
Delinquency	0.03 (0.02-0.04)	9.7%
Alcohol consumption	0.06 (0.04-0.09)	17.3%
Friends' alcohol consumption	0.04 (0.02-0.05)	10.9%

Table 3. Effect of each mediation term on estimated association between ADHD symptoms and AUD.

	Odds ratio (95% CI)
<i>Before adjusting for mediators</i>	
Unadjusted	1.97 (1.55-2.50)
Adjusted for confounders	1.61 (1.26-2.05)
<i>Adjusted for each mediator</i>	
Adjusted for depressive symptoms	1.94 (1.53-2.45)
Adjusted for delinquency	1.74 (1.36-2.21)
Adjusted for adolescent alcohol consumption	1.86 (1.45-2.39)
Adjusted for friends' alcohol consumption	1.81 (1.44-2.29)
<i>Adjusted for two mediators</i>	
Adjusted for delinquency and alcohol consumption	1.72 (1.34-2.20)
<i>Fully adjusted model</i>	
Adjusted for delinquency and alcohol consumption, and confounders	1.47 (1.15-1.89)

Table 4. Results of multiple mediator model.

	Indirect effect of mediation (ab) and 95% CI	Proportion of total effect mediated
Delinquency	0.03 (0.02-0.04)	8.0%
Drink alcohol	0.04 (0.02-0.06)	11.0%
Total	0.07 (0.02-0.11)	19.0%

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Chapter 5 (Paper 3): The Joint Effects of Childhood

Hyperactivity/Impulsivity and Maltreatment/Neglect on Adult Alcohol Use Disorder

Background

Stressful life events in childhood, such as maltreatment/neglect or mental health conditions, have been shown to have cumulative long lasting effects on mental and physical health in adulthood. The purpose of this study was to examine the joint effects of two life events associated with stress, childhood Attention Deficit Hyperactivity Disorder (ADHD) symptoms and maltreatment/neglect, on adult alcohol use disorder (AUD).

Methods

Weighted logistic regression was used to examine the association between retrospective reports of childhood ADHD symptoms and maltreatment/neglect with adult AUD in a nationally representative sample of 11,038 participants in the National Longitudinal Study of Adolescent to Adult Health.

Results

Those meeting criteria for one or both ADHD domains had almost twice the odds of adulthood alcohol dependence compared with those who did not (odds ratio [OR] = 1.97, 95% confidence interval [CI] = 1.55-2.50). This association was partially attenuated after adjusting for sex, race/ethnicity, parental AUD, and maltreatment/neglect (AOR = 1.61, 95% CI = 1.26-2.05). The effect was slightly stronger for those with hyperactivity/impulsivity symptoms than those with inattention symptoms. There was no

strong evidence for multiplicative interaction by child maltreatment/neglect, sex, or parental AUD.

Conclusions

Childhood ADHD symptoms may be a risk factor for AUD in adulthood. This study has implications for identify and monitor children with ADHD symptoms to prevent later onset of AUD.

Keywords: ADHD, Alcohol use disorder, Maltreatment, Neglect, Adolescent health

5.1. Introduction

AUD represents a large public health burden. According to National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) data, 8.5% of adults over 18 had experienced AUD in the past year (4.7% abuse, 3.8% dependence), and 30.3% had experienced AUD in their lifetime (17.8% abuse, 12.5% dependence; Hasin et al., 2007). Alcohol abuse is associated with preventable health problems such as cirrhosis of the liver and increased risk of injury/fatality. Alcohol is reported to be the third leading cause of death in the U.S., after tobacco and poor diet/physical inactivity (Mokdad et al., 2004). AUD treatment is expensive and time consuming, with unsatisfactory efficacy rates (Ferri et al., 2006). Thus research on precursors and risk factors of AUD is beneficial to recognizing red flags and opportunities for intervention in adolescence, to prevent AUD and related health consequences in adulthood.

The Life Course Perspective describes how events and environmental factors shape personality and behavior throughout the lifespan. It is a useful framework for studying AUD, because of the dynamic nature of alcohol use behaviors and their risk factors (Hser et al., 2007); in other words, abusing alcohol is not an event that happens at one point in time, but a behavior that changes over time, and may be influenced by past and current life events. Early adversity and toxic stress contribute to adulthood disease, affecting the developing brain architecture as well as the coping/stress responses to future adversity (Shonkoff et al., 2012). Research has shown that experiencing adverse events such as maltreatment and neglect in childhood may be associated with later AUD (Enoch, 2011; Hser, et al., 2007), and experiencing multiple adverse events carries more risk

(Dube et al., 2002). This relationship may be partly due to using alcohol to cope with or escape from trauma and related depressive symptoms, reduce feelings of isolation and loneliness, self-medicate in an attempt to gain control over the experience, and improve self-esteem (Widom & Hiller-Sturmhofel, 2001).

Another type of childhood adversity stems from the consequences of having a mental health condition such as Attention Deficit Hyperactivity Disorder (ADHD). Children with ADHD display symptoms of attentional difficulties and/or hyperactivity/impulsivity (American Psychiatric Association, 2000), which can affect interpersonal relationships and behavior at school and home, and can persist into adulthood (Barkley, 2014). A child with ADHD symptoms may experience negative events such as getting into trouble at home and at school, getting poor grades, or being bullied by peers. Children diagnosed with ADHD may be more likely to experience AUD later in life, possibly due to using alcohol as a calming agent to counteract hyperactivity, or using alcohol as a maladaptive coping mechanism to deal with stresses and negative experiences resulting from ADHD (Barkley, 2014). In addition, qualitative research suggests that individuals with ADHD may use alcohol to obtain a sense of belongingness with peers (Nehlin et al, 2015). However, this can have important negative consequences into adulthood. In a recent meta-analysis of ten cohort studies of 3,184 participants, authors found that childhood ADHD was associated with 35% higher odds (95% CI: 11-64%) of alcohol abuse in young adulthood (Charach et al., 2011). However, in four of the ten studies, the AUD outcome was measured at the mean age of 18 years, which is too young to assess the lifetime risk of developing AUD. This meta-analysis also did not separate alcohol abuse from dependence outcomes. In addition, most studies don't take

into account confounding or moderating relationships with variables such as childhood maltreatment, which has been purported to be associated with both ADHD (Ouyang et al., 2008; World Health Organization, 2016) and AUD (Dube et al., 2002; Shin et al., 2009). Sex may also play a confounding or moderating role, as males are more likely to be diagnosed with ADHD (Akinbami, et al., 2011) as well as AUD (SAMHSA, 2004). Reasons for using for alcohol, rates of comorbidities, and treatment response may also vary by sex (Brady & Randall, 1999).

Therefore, literature about ADHD and AUD in adulthood is lacking with regards to high quality prospective studies that account for important confounding and moderating variables, and cumulative effects of multiple negative exposures. This study aimed to assess the association between ADHD symptoms and adulthood AUD, while accounting for factors such as parental AUD and childhood maltreatment. We hypothesized that ADHD symptoms would be positively associated with adulthood AUD, and that this association would vary by sex and by childhood maltreatment experience. We hypothesized that the primary association would be stronger for males than females, due to males' increased risk for both ADHD symptoms and AUD. We also hypothesized that we would find evidence of joint effects of ADHD symptoms and maltreatment experience, as assessed by the presence of multiplicative interaction, due to the cumulative effect of multiple adverse events in childhood.

5.2. Methods

5.2.1. Dataset

This study was a secondary data analysis of Waves I, III, and IV of the National Longitudinal Study of Adolescent to Adult Health (Add Health; UNC Carolina Population Center, 2011). The Add Health study used a multistage stratified cluster design and included four waves of data collection from adolescence to adulthood. Data were collected using in person interview, as well as computer-assisted self-interview for sensitive questions. In total, 12,288 participants had data and sample weights for Waves I (mean age 15.4), III (mean age 21.8), and IV (mean age 28.3). Cases were excluded from analyses if they were missing data for the independent variable or outcome variable, leaving an analytic sample size of 11,038.

5.2.2. Measures

5.2.2.1. Dependent variable

Questions about use, frequency, amount, and consequences of alcohol consumption were used to construct a variable measuring lifetime alcohol abuse (harmful use of alcohol) and dependence (harmful use plus physical dependency symptoms or being unable to quit drinking) at Wave IV. These questions were based on DSM criteria for alcohol abuse and dependence. DSM-IV criteria for alcohol abuse includes recurrent alcohol use impairing performance at work, home or school, recurrent alcohol use in situations in which it is physically hazardous (e.g. driving, etc.), recurrent alcohol-related legal problems, and continued use despite social or interpersonal problems due to alcohol use (e.g. fighting with one's spouse). DSM-IV criteria for alcohol dependence include increasing tolerance to alcohol, withdrawal symptoms after stopping use, using more alcohol than intended, unsuccessful attempts to quit, spending a lot of time obtaining,

using, and recovering from alcohol, giving up activities because of alcohol use, and continued use after knowledge of recurrent physical or psychological sequelae (American Psychiatric Association, 2000). The Add Health team classified participants into three groups: No abuse/dependence (72.6%), DSM-IV abuse diagnosis (12.9%), or DSM-IV dependence diagnosis with or without physiological symptoms (14.5%). Answering positively to one of the abuse symptoms, or three of the dependence symptoms (with special emphasis on tolerance and withdrawal), classified the participant as positive for alcohol abuse and/or dependence. This variable was measured at Wave IV, in the third decade of life (mean age 28.3 years); therefore this measure is likely to identify most individuals who will develop AUD, because previous literature indicates that the mean age of onset is about 22 years of age and the hazard rate of onset peaks around 19 years of age (Hasin et al., 2007). Due to the Add Health questionnaire skip patterns, about 59.4% of the sample skipped some alcohol-related questions. These cases were considered to be light drinkers and non-drinkers, and they were classified as no abuse or dependence for analysis purposes.

5.2.2.2. Independent variables

ADHD symptoms were assessed retrospectively at Wave III with 17 questions about the respondent's behavior between 5 and 12 years of age, dichotomized into two domains, hyperactivity/impulsivity (HI) and inattention (IN). Wording and choice of questions reflect DSM-IV criteria for clinician diagnosis of ADHD, with two exceptions. The DSM-IV impulsivity symptom of "Often interrupts or intrudes on others (e.g., butts into conversations or games)" was not included on the Add Health questionnaire. "You were spiteful or vindictive" was asked instead, which is not a DSM-IV symptom and

therefore was excluded from current analyses, resulting in a total of 8 HI symptoms and 9 IN symptoms. Each question had the following response options: never or rarely, sometimes, often, or very often. Following the precedent set by Kollins et al., 2005, a response of often or very often was coded as a positive response. A cutoff of six symptoms was used for each domain, consistent with DSM-IV criteria. Respondents were classified into two ADHD groups: (1) met criteria for one or both domains (≥ 6 HI symptoms and/or ≥ 6 IN symptoms), and (2) did not meet criteria for either domain (< 6 HI and < 6 IN symptoms).

Maltreatment experience (physical and sexual) before entering sixth grade was assessed retrospectively at Wave III. Reporting one or more occurrences of physical maltreatment was coded as having experienced some physical maltreatment; sexual maltreatment was coded in the same way. Supervisory and/or physical neglect was also measured retrospectively. Following previous literature, childhood neglect was coded as at least six instances of being left home alone and/or at least one instance of neglecting basic needs (Fang & Corso, 2007). Participants who met criteria for any of these three variables were considered to have experienced “any maltreatment” in analyses.

5.2.2.3. Confounders

Self-reported race/ethnicity of the participant was coded as follows: non-Hispanic White, non-Hispanic Black, Hispanic, Asian, or Other. Parental AUD was coded as having at least one biological parent with AUD, as reported by a parent at Wave I. Participant sex was self-reported.

5.2.3. Statistical analysis

Participants with missing data for independent, moderating, or outcome variables were excluded from analyses. Dummy variables were created to account for missing data for the variables race/ethnicity (0.3%) and parental AUD (12.7%).

PROC SURVEYLOGISTIC (SAS version 9.3; Cary, NC) was used to conduct logistic regression analysis with the outcome variable, AUD, in two ways: alcohol abuse and/or dependence, and alcohol dependence alone. Predicted probabilities were calculated when the prevalence of the outcome was greater than 10%. The presence of multiplicative interaction by childhood maltreatment (any maltreatment including physical, sexual, or neglect) was assessed by comparison of observed and expected joint effects, assessment of homogeneity of stratum-specific effect estimates, and testing of interaction terms in regression models. Sex and parental AUD were also examined as potential moderators. Confounders included sex, race/ethnicity, and parental AUD. Sample weights were applied to all analyses to account for the complex sample design.

5.3. Results

5.3.1. Descriptive statistics

Descriptive statistics can be found in Tables 1-2. At Wave I, the sample had a mean age of 15.4 years (standard deviation: 0.1) and was 47.9% male. Race/ethnicity composition was as follows: 69.3% white, 14.9% African American, 11.4% Hispanic, 3.3% Asian, and 0.7% American Indian/Native American. Regarding AUD, 24.8% of the sample met criteria for either abuse or dependence at Wave IV, and 14.5% met criteria for dependence. These rates are fairly similar to previous research, which reported that

about 30% of adults had experienced AUD in their lifetime, including 13% who had experienced alcohol dependence (Hasin et al., 2007).

Those with AUD at Wave IV were significantly more likely to be male and white. Approximately eight percent of the sample met criteria for one or both domains of ADHD symptoms. Those who met ADHD criteria were more likely to meet criteria for abuse or dependence than those who did not (10.6% vs. 7.3%; $p < .0001$), and more likely to meet criteria for dependence than those who did not (13.5% vs. 7.3%; $p < .0001$).

Regarding childhood maltreatment, 28.3% of the sample reported experiencing physical maltreatment, 4.8% reported sexual maltreatment, and 19.5% reported neglect. Those reporting physical abuse were more likely to meet criteria for AUD, whether defined by abuse/dependence or dependence only (p 's $< .05$). The difference in proportion of those who experienced sexual maltreatment and neglect by AUD status (abuse or dependence) was marginally significant ($p = .0784$ and $p = .0661$, respectively). The difference in proportion of those who experienced neglect by AUD status (dependence) was statistically significant ($p = .0043$).

5.3.2. Association between ADHD symptoms and AUD

Meeting criteria for one or both ADHD domains was significantly associated with a greater predicted probability (35.3% vs. 26.7%; $p < .0001$) and greater odds (OR=1.50, 95% CI: 1.22-1.84) of meeting criteria for AUD abuse or dependence, compared to participants who did not meet criteria for either domain (see Table 3).). Subsequent confounder testing showed that sex had the largest confounding effect, causing the effect estimate to change by 8.8%. Therefore, the fully adjusted model included the following confounders: sex, race/ethnicity, any maltreatment, and parental AUD. In the fully

adjusted model, those who met criteria for one or both ADHD domains had a greater predicted probability of AUD abuse or dependence compared with those who did not, while holding the values of confounders to 0 (33.3% vs. 24.5%; $p<.0001$). The odds ratio was marginally significant (AOR=1.21, 95% CI: 0.98-1.49, $p=.071$). The association was slightly stronger for participants who met criteria for hyperactivity/impulsivity (AOR=1.62, 95% CI: 1.22-2.16) than for participants who met criteria for inattention (AOR=1.22, 95% CI: 0.84-1.77), when compared to participants who did not meet ADHD domain criteria.

As shown in Table 4, meeting criteria for one or both ADHD criteria was significantly associated with a greater predicted probability of AUD dependence. Those meeting criteria for ADHD had a greater predicted probability of dependence compared to those who did not (23.8% vs. 13.6%; $p<.0001$), or 1.97 times higher odds (95% CI: 1.55-2.50) in the unadjusted model. Adjusting for confounders (e.g., holding all confounder values set to 0) resulted in greater predicted probabilities of 22.4% for those meeting criteria for ADHD compared to 12.6% for those who did not ($p<.0001$), or 1.61 times higher odds (95% CI: 1.26-2.05). Confounder testing resulted in the selection of the same confounders as previously included, and again sex had the largest effect on the effect estimate (9.6%). Again the effect was slightly stronger for participants who met criteria for hyperactivity/impulsivity (AOR=1.96, 95% CI: 1.41-2.74) than for participants who met criteria for inattention (AOR=1.73, 95% CI: 1.16-2.57; results not shown), compared to participants who did not meet criteria for these domains.

5.3.3. Effect modification analyses

There was no evidence of interaction by any maltreatment; the interaction term was not statistically significant ($p=.8835$), and the observed joint OR (1.86; 95% CI: 1.37-2.51) did not vary greatly from the product of the odds ratios (2.19). In addition, the effect estimates did not vary by stratum of maltreatment (1.56 vs. 1.65).

The interaction term was not statistically significant for either sex ($p=.4919$) or parental AUD in either model ($p=.7348$). However, stratification of the association by sex resulted in different effect estimates; the association between ADHD symptoms and alcohol dependence was slightly stronger for males (AOR=1.84, 95% CI: 1.17-2.88) than for females (AOR=1.50, 95% CI: 1.13-1.97), indicating the possibility of multiplicative interaction. There was no evidence of interaction by parental AUD.

5.4. Discussion

ADHD symptoms during childhood were associated with 61% increased odds of alcohol dependence during adulthood, after adjusting for confounders. These results are consistent with previous literature that found increased risk of AUD in young adulthood. Charach and colleagues (2011) reported ten studies with odds ratios ranging from 0.60 to 2.24, and a pooled odds ratio of 1.35 (95% CI: 1.11-1.64). However, the adjusted model was not significant for the less stringent outcome of abuse or dependence, which may indicate that ADHD symptoms are more associated with symptoms of physical dependence than with abuse. This subtle distinction is not apparent in previous literature such as the above meta-analysis, because abuse and dependence are usually considered together. Additionally, the main association was slightly stronger when comparing participants who met criteria for the hyperactivity/impulsivity ADHD domain to those who met criteria for neither domain; the effect was still present when comparing participants who criteria for the inattention ADHD domain to those who met criteria for neither domain, but only for the alcohol dependence outcome. This finding has not been reported previously to our knowledge.

Some previous research suggests a bidirectional association between maltreatment and ADHD (Ouyang et al., 2008); mistreated children may display behavioral symptoms mimicking those of ADHD, and conversely, ADHD symptoms may increase chances of maltreatment from adults due to misbehavior (Barnett, et al., 2005). However, childhood maltreatment and neglect are not always considered when assessing the association between ADHD symptoms and AUD. This is an important consideration due to the relationships between maltreatment/neglect and ADHD symptoms, and between

maltreatment/neglect and AUD. We sought to examine the joint effects of multiple negative exposures, child maltreatment/neglect and ADHD symptoms, on the odds of adult AUD. However, multiplicative interaction by maltreatment/neglect or parental AUD was not observed as hypothesized; instead, maltreatment/neglect played a confounding role in the main association. Inclusion of the any maltreatment or neglect variable resulted in a decrease in the main effect estimate. This study was not able to find evidence of interaction or examine the temporal sequence between ADHD and maltreatment; we believe that the relationships between these variables need further examination in future research.

Confounders were carefully selected for the fully adjusted models based on theoretical importance and effect on the effect estimate. Sex, race/ethnicity, maltreatment or neglect, and parental AUD caused the largest changes in the effect estimate. Sex had the largest confounding effect, likely because the prevalence of ADHD and AUD both differ by sex. Other confounders were considered, including age at Wave I, parental socioeconomic status (measured by maternal education and trouble paying bills), and household structure; however, these variables did not have much effect on the effect estimate. Some evidence of effect modification by sex was observed in stratification analyses, although this interaction was not statistically significant. As hypothesized, the association between ADHD symptoms and AUD was slightly stronger for males than females, which may suggest multiplicative interaction. However, the interaction term was not statistically significant; therefore, we cannot conclude that this observation is proof of multiplicative interaction. It was difficult to assess interaction by parental AUD due to

the small number of participants who had a reported parent with AUD. More research is needed to explore these possible interaction effects.

The association between childhood ADHD symptoms and adult AUD highlights the importance of childhood individual and environmental characteristics as influences on adult mental health. The Life Course Perspective purports that adverse or negative events in childhood can have long lasting negative effects on mental and physical health; thus a child who may experience negative consequences as a result of ADHD symptoms (such as frequently getting in trouble at school or having trouble making friends) might develop maladaptive behavior patterns and mental health disorders later in life. For example, children with ADHD symptoms may seek early alcohol use in adolescence to calm hyperactive symptoms, which would be supported by our finding that the association was stronger for those meeting criteria for hyperactivity/impulsivity. These adolescents may also engage in underage drinking to seek a sense of belonging with peers (Nehlin, 2015). These individuals may be at increased risk for conduct disorder and increased exposure to deviant peers and early access to alcohol as an adolescent (de Sanctis et al., 2008); this may then serve as a mechanism to increased risk of AUD in adulthood (Looby, 2008). Further study is needed to further clarify the mechanisms responsible for the association between childhood ADHD and adulthood AUD, such as adolescent delinquency.

The limitations of this study mostly pertain to the Add Health study design. The retrospective measurement of childhood maltreatment and ADHD symptoms may be vulnerable to measurement/recall bias. However, self-reported ADHD symptoms may be a more sensitive measure than clinical diagnosis, as it may catch more subclinical cases. In addition, self-reported AUD may be vulnerable to bias, if participants were untruthful

about AUD symptoms due to embarrassment. We also note that there may be “diagnostic orphans” with some AUD or ADHD symptoms, who did not have enough symptoms to meet domain criteria; these individuals were classified in the same group with participants without any AUD or ADHD symptoms. Despite the above limitations, this study also has strengths. The Add Health dataset is a large, nationally representative dataset with a large sample size and a longitudinal design following participants from adolescence to adulthood. The analyses are weighted using sample weights provided, meaning that the conclusions drawn from this study can be generalized to all American adolescents and adults.

Previous literature regarding the association between childhood ADHD and adulthood AUD was limited (Charach et al., 2011); most articles included an outcome variable of AUD including abuse, measured early in life. There were few articles that examined ADHD symptoms as an independent variable, or examined AUD measured in adulthood. This study adds to the existing literature by examining the independent variable of ADHD symptoms and the outcome of alcohol dependence, which is a different construct than alcohol abuse. Dependence is defined by the presence of physical symptoms such as withdrawal, while abuse refers to overconsumption of alcohol, which may often be a consequence of social environment more than a mental health disorder. In addition, the AUD outcome was measured later in adulthood than in previous literature, which often measured alcohol usage at age 18, which may not be representative of an individual’s lifetime alcohol use. Finally, effect modification by childhood maltreatment, sex, and parental AUD was explored, which was lacking in previous literature.

5.5. Conclusions

The results of this study have implications for lasting mental health effects and AUD in adulthood. Children with ADHD symptoms or diagnoses may need extra support, from a school psychologist or other professionals, to reduce the risk of developing maladaptive coping behaviors such as binge drinking. Future research may further examine causal pathways in this relationship, with an eye toward methods of reducing risk of AUD. Childhood maltreatment should be considered in epidemiological studies of ADHD and AUD, and when evaluating a child with behavioral symptoms such as those of ADHD.

Conflict of Interest

The authors have no conflicts of interest to report.

5.6. Tables and Figures

Figure 1. Conceptual Framework

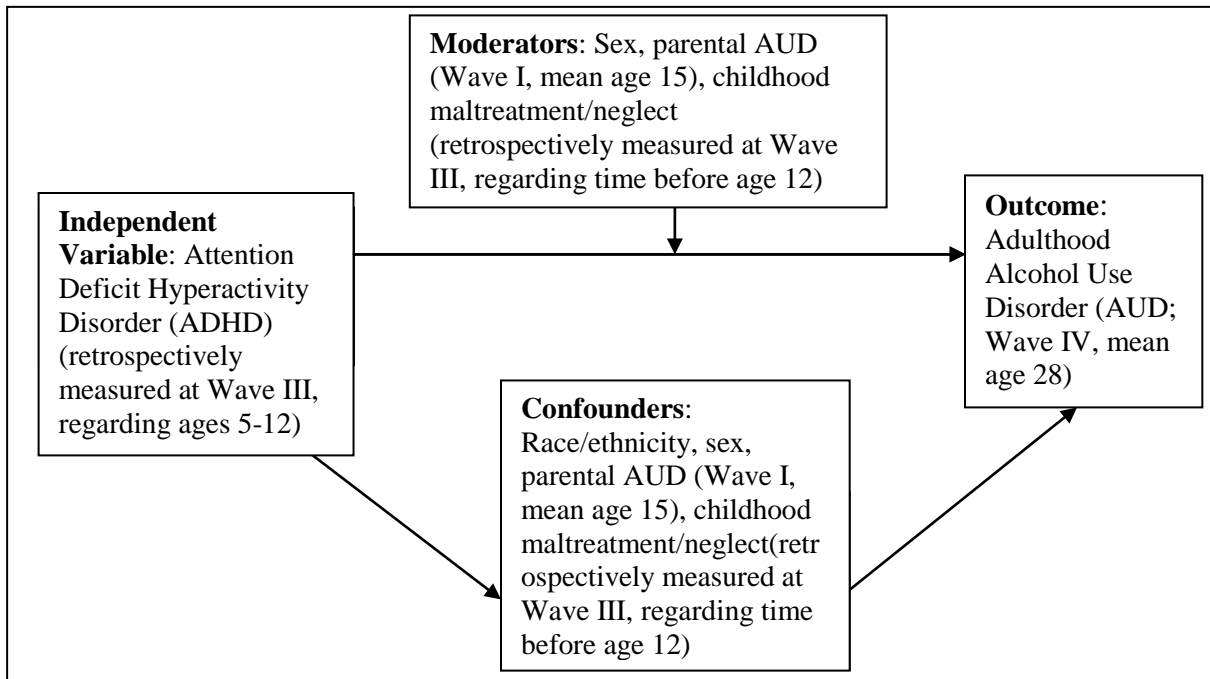


Table 1. Descriptive characteristics of sample (unweighted numbers, weighted percentages) by AUD outcome (abuse or dependence).

	Total (n=11,038)	No alcohol use disorder (n=8,296; 75.2%)	Alcohol use disorder (n=2,742; 24.8%)	p value
Sex (n, weighted %)				<.0001
Male	4,901 (47.9)	3,381 (44.2)	1,520 (57.5)	
Female	6,137 (52.1)	4,915 (55.8)	1,222 (42.5)	
Race/ethnicity				<.0001
White	6,240 (69.3)	4,250 (65.0)	1,990 (80.9)	
African American	2,302 (14.9)	2,026 (18.1)	276 (6.4)	
Hispanic	1,689 (11.4)	1,371 (12.4)	318 (8.7)	
Asian	685 (3.3)	566 (3.5)	119 (2.8)	
American Indian/Native American	93 (0.7)	65 (0.7)	28 (0.8)	
Missing	29 (0.3)	18 (0.2)	11 (0.3)	
Parental AUD				.0105
Either biological parent	279 (2.8)	192 (2.5)	87 (3.8)	
Neither biological parent	9,027 (84.5)	6,773 (84.7)	2,254 (84.2)	
Missing	1,732 (12.7)	1,331 (12.9)	401 (12.0)	
Child maltreatment				
Sexual	540 (4.8)	422 (5.1)	118 (3.9)	.0784
Physical	3,245 (28.3)	2,266 (26.6)	979 (33.0)	<.0001
Neglect	2,173 (19.5)	1,582 (18.9)	591 (21.1)	.0661
Any maltreatment	4,261 (37.9)	3,026 (36.0)	1,235 (43.0)	<.0001
ADHD Symptoms				<.0001
Meets neither cutoff	10,207 (91.8)	7,755 (92.7)	2,452 (89.4)	
Meets either cutoff	831 (8.2)	541 (7.3)	290 (10.6)	

*Between group differences were tested by PROC SURVEYFREQ (Chi Square test).

Table 2. Descriptive characteristics of sample (unweighted numbers, weighted percentages) by AUD outcome (dependence).

	Total (n=11,038)	No alcohol use disorder (n=9,592; 85.5%)	Alcohol use disorder (n=1,446; 14.5%)	p value
Sex (n, weighted %)				<.0001
Male	4,901 (47.9)	4,060 (45.6)	841 (61.1)	
Female	6,137 (52.1)	5,532 (54.4)	605 (38.9)	
Race/ethnicity				<.0001
White	6,240 (69.3)	5,195 (67.4)	1,045 (80.8)	
African American	2,302 (14.9)	2,161 (16.4)	141 (6.1)	
Hispanic	1,689 (11.4)	1,522 (11.8)	167 (8.8)	
Asian	685 (3.3)	612 (3.3)	73 (3.2)	
American Indian/Native American	93 (0.7)	77 (0.7)	16 (1.0)	
Missing	29 (0.3)	25 (0.3)	4 (0.1)	
Parental AUD				.0049
Either biological parent	279 (2.8)	226 (2.6)	53 (4.6)	
Neither biological parent	9,027 (84.5)	7,849 (84.8)	1,178 (83.0)	
Missing	1,732 (12.7)	1,517 (12.7)	215 (12.4)	
Child maltreatment				
Sexual	540 (4.8)	470 (4.2)	70 (3.8)	.1448
Physical	3,245 (28.3)	2,716 (27.6)	529 (32.4)	.0119
Neglect	2,173 (19.5)	1,819 (18.8)	354 (23.2)	.0043
Any maltreatment	4,261 (37.9)	3,577 (36.9)	684 (43.5)	.0013
ADHD Symptoms				<.0001
Meets neither cutoff	10,207 (91.8)	8,946 (92.7)	1,261 (86.5)	
Meets either cutoff	831 (8.2)	646 (7.3)	185 (13.5)	

*Between group differences were tested by PROC SURVEYFREQ (Chi Square test).

Table 3. Association between ADHD symptoms and adult AUD (abuse or dependence).

	Unadjusted model; OR (95% CI)	Adjusted Model; AOR (95% CI)
ADHD group		
Meets neither cutoff	Ref	Ref
Meets either cutoff	1.50 (1.22-1.84)	1.21 (0.98-1.49)
Sex		
Female		Ref
Male		1.69 (1.51-1.89)
Race/ethnicity		
White		Ref
African American		0.28 (0.22-0.36)
Hispanic		0.54 (0.43-0.67)
Asian		0.60 (0.42-0.87)
American Indian/Native American		0.85 (0.48-1.50)
Parental AUD		
Neither biological parent		Ref
Either biological parent		1.52 (1.10-2.10)
Child maltreatment		
No maltreatment or neglect		Ref
Maltreatment or neglect		1.36 (1.19-1.54)

Table 4. Association between ADHD symptoms and adult AUD (dependence).

	Unadjusted model; OR (95% CI)	Adjusted Model; AOR (95% CI)
ADHD group		
Meets neither cutoff	Ref	Ref
Meets either cutoff	1.97 (1.55-2.50)	1.61 (1.26-2.05)
Sex		
Female		Ref
Male		1.81 (1.58-2.06)
Race/ethnicity		
White		Ref
African American		0.31 (0.23-0.42)
Hispanic		0.61 (0.46-0.79)
Asian		0.78 (0.48-1.26)
American Indian/Native American		1.02 (0.55-1.89)
Parental AUD		
Neither biological parent		Ref
Either biological parent		1.78 (1.18-2.68)
Child maltreatment		
No maltreatment or neglect		Ref
Maltreatment or neglect		1.28 (1.08-1.52)

5.7. References

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Chapter 6: Conclusions

6.1 Main Findings

In Paper 1, we observed that individuals who reported sexual maltreatment were 34% more likely to be obese and 72% more likely to be extremely obese in adulthood. Individuals who reported physical maltreatment were 37% more likely to be extremely obese. Physical maltreatment was also associated with self-rated weight status in adulthood, but sexual maltreatment was not. The association between physical and sexual maltreatment in childhood and extreme obesity in adulthood was partially mediated by adolescent depressive symptoms and adolescent BMI. We concluded that a child who is mistreated or neglect may be likely to show signs of depression or overeating by adolescence, which may be linked with extreme obesity later in life.

In Paper 2, we observed that adolescent delinquent behavior, adolescent alcohol consumption and friends' alcohol consumption were all statistically significant mediators in the pathway between childhood ADHD symptoms and adulthood AUD. Statistical adjustment for delinquent behavior and alcohol consumption caused the main association between ADHD symptoms and AUD to decrease by about 20%. Therefore, a child with ADHD symptoms may be more likely to develop maladaptive coping methods such as delinquent behavior (including drinking alcohol) in adolescence, increasing risk for AUD in adulthood.

In Paper 3, we observed that individuals meeting criteria for one or both ADHD domains had higher odds of adulthood alcohol abuse and/or dependence. Interestingly, the effect was slightly stronger for those with hyperactivity/impulsivity symptoms than

those with inattention symptoms, which could possibly indicate that individuals use alcohol to calm hyperactive symptoms. We did not find evidence of multiplicative interaction to indicate joint effects of ADHD symptoms and physical maltreatment or neglect, as hypothesized. Although effect modification analyses did not show statistical significance, there was some evidence of multiplicative interaction by sex, in other words, that this association was somewhat stronger for males than for females. Therefore, we concluded that childhood ADHD symptoms may be a risk factor for AUD in adulthood. The strengths of the associations observed in Papers 1 and 3 were roughly similar (odds ratios between 1.3-2.0); thus we know that these associations are present, but we also know that experiencing maltreatment or ADHD symptoms in childhood doesn't necessarily guarantee poorer adult health outcomes. Rather, there is opportunity for intervention or self-directed change during childhood, adolescence, and early adulthood, to overcome such obstacles.

Taken together, these three papers greatly support the idea of the Lifecourse Perspective, which served as the main theoretical framework for this research project. That is, stressful life events in childhood were associated with specific behaviors and symptoms in adolescence, as well as poorer health outcomes in adulthood. It is evident that an individual's health in adulthood must be observed in the context of the changing social environment present throughout the individual's life. We observed that social factors such as experiencing maltreatment or having adolescent friends who consume alcohol were associated with compensatory behaviors and poorer health outcomes much later in life, as much as individual characteristics such as ADHD symptoms or the individual's adolescent alcohol consumption. Therefore, we argue that the sum of one's

experiences throughout the life course, whether mental, physical, or social, greatly impact the individual's long-term state of health.

6.2. Additional and Future Research

In considering the results of the three papers together, it becomes apparent the two outcome measures, obesity and AUD, share some similarities that cannot be ignored. Both may represent a compensatory process or maladaptive coping mechanism to deal with stress, dull negative feelings, or fill an emotional “hole.” It is worth noting that approximately 9.3% of the sample in this study met criteria for both alcohol abuse or dependence *and* obesity ($BMI \geq 30 \text{ kg/m}^2$); about 25% of obese participants met criteria for AUD, and 34% of those who met criteria for AUD were obese. Testing a joint outcome of obesity and AUD resulted in similar the following effect estimates, by independent variable: ADHD symptoms (AOR=1.39, 95% CI: 1.03-1.86), physical maltreatment (AOR=1.32, 95% CI: 1.10-1.59), sexual maltreatment (AOR=0.99, 95% CI: 0.64-1.53), and neglect (AOR=1.20, 95% CI: 0.95-1.52). We see that ADHD symptoms and physical maltreatment are both associated with the joint outcome, and the strength of the associations is roughly similar to what was observed in Papers 1 and 3. There may be a stronger effect with more stringent criteria (alcohol dependence and extreme obesity); however, the lower prevalence of this more stringent outcome results in unstable effect estimates. Future research into mechanisms that contribute to comorbid health outcomes, AUD and obesity, may prove interesting and is not common in the literature.

The results of this project may suggest other research questions as well. For example, further research could test these associations with other similar mental health

outcomes, such as drug use and abuse. Secondly, one limitation of the current project was that the Add Health questions about maltreatment and ADHD symptoms both included a sizeable age range (before age 12, and between ages 5-12), precluding any assessment of temporal relationship between the two to determine which occurred first. Future research could use more sensitive measures to closely examine this relationship. Thirdly, the role of ADHD medication was not addressed by this project; future research could assess whether treatment (pharmacological or psychological) buffers some negative effects of ADHD symptoms. Additionally, Wave V data collection is planned to take place in 2016-2018, as the participants reach their fourth decade of life, providing an opportunity to study the durability of the health outcomes. Wave V will also collect data on causes of death; participants who have died as a result of their AUD or extreme obesity could be considered as another health outcome, although presumably rare at the fourth decade of life. This project also lent some support to the hypothesis of the heritability of AUD from parent to child; in Paper 3, having at least one parent with AUD was associated with greater odds of meeting criteria for AUD at Wave IV. One possible extension of this project would be to study the children of the Add Health participants, to document the next generation's likelihood of repeating patterns of AUD as well as other mental health conditions. Finally, as with any epidemiological research, it is necessary to test these findings in other datasets as well as other populations, to test their external validity.

6.3. Public Health Significance and Implications

This dissertation has several implications for future epidemiological research. First, a common finding throughout all three papers was that using different cutoffs or thresholds of exposure and outcome variables noticeably changed the results of the

analyses. For example, physical maltreatment was not significantly associated with $\text{BMI} \geq 30 \text{ kg/m}^2$, but was significantly associated with $\text{BMI} \geq 40 \text{ kg/m}^2$. Similarly, ADHD symptoms were more strongly associated with an alcohol dependence outcome than with alcohol abuse or dependence. In both cases, the more stringent outcome possibly represented a more serious disorder; i.e., not just a social heavy drinker but someone physically dependent on alcohol, and not just an overweight person (as is more and more common in the past couple decades) but someone with a serious problem with overeating. These findings illustrate the importance of exploring multiple ways of operationalizing variables, based on not only previous literature, but also the theoretical framework and study hypotheses.

Secondly, the use of the MacKinnon method of testing mediation proved to be a useful method to measure mediation that offers one large advantage over other methods of mediation analysis. Whereas the traditional method by Baron and Kenny is considered to be a causal steps approach, MacKinnon uses a product of coefficients approach to calculate a direct estimate of the indirect effect of mediation. The indirect effect of mediation can be quantitatively measured along a continuum rather than only detecting present, absent, or partial mediation; this allows comparisons between mediating variables as well as statistical hypothesis testing. In addition, a multiple mediator model can be constructed, to allow for more sophisticated conceptual models. Although some cumbersome calculation is required, the advantages of this method are great. Therefore, future epidemiological researchers are recommended to explore use of the MacKinnon method of testing mediation.

The results of this research increase our understanding of the longitudinal relationships between stressful events in childhood, adolescent characteristics and behaviors, and adult mental and physical health, which has significant implications for mental health professionals who treat individuals across the lifespan. It is crucially important to treat the “whole self” and consider an individual’s history (i.e., comorbidities such as depression or ADHD), as well as family history (such as parental AUD) and social relationships (including possibility of maltreatment or neglect) when treating a patient who presents with behaviors such as binge eating or alcohol abuse. Otherwise, treatment may be more likely to fail if the individual has not dealt with past stress or trauma.

Regarding the sensitive development stages of childhood and adolescence, policymakers must consider methods to reduce the incidence of childhood trauma such as maltreatment and neglect, by considering the importance of community for both children and their parents. Possible cases of maltreatment or neglect must be thoroughly investigated whenever suspected by those in the community, in order to spare the child additional insult. Pediatricians and community leaders may be positioned to consider preventive measures to prevent toxic stress exposures for children and adolescents, within the ecobiodevelopmental framework as suggested by previous authors (Shonkoff, et al, 2012). Current community programs such as those for mandated reporting by educators and law enforcement, screenings for mothers with postpartum depression, subsidized childcare for parents with limited resources, and subsidized lunches for children at school, can all help to reduce the overall incidence of child maltreatment and neglect. The

larger community must continue to develop infrastructure to prevent as many cases of maltreatment and neglect as possible.

Likewise, these results highlight the opportunity for intervention for children and adolescents who show early signs of obesity, ADHD symptoms, depressive symptoms, or delinquent behavior, especially alcohol consumption. An adolescent with depressive symptoms is not only at risk for further depression, but could also be at risk for other poor health outcomes such as obesity. Professionals such as social workers, school psychologists, and teachers are positioned to take note of these warning behaviors or changes in behavior, and seek treatment for the child. Suspected cases of ADHD must be diagnosed and treated accordingly with behavioral as well as pharmaceutical therapies. School teachers and authority figures should consider that some adolescents who display delinquent behavior could be acting out as a result of an undiagnosed problem such as ADHD. Likewise, adolescents who already meet criteria for obesity should be referred to the appropriate resources to learn about diet and exercise, but they may also benefit from an appointment with a psychologist or social worker to investigate possible root causes (including maltreatment or neglect). Health outcomes such as obesity and AUD cost America billions of dollars annually in healthcare costs, and do unquantifiable damage to quality of life; any opportunity to decrease these public health burdens must be seized upon.

Chapter 7: References

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