

## ABSTRACT

Title of thesis: LONGITUDINAL ASSOCIATIONS BETWEEN METHAMPHETAMINE USE AND DEPRESSION AMONG YOUNG ADULTS IN THE UNITED STATES: A SECONDARY ANALYSIS

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Methamphetamine is a powerful, highly addictive central nervous system stimulant that is associated with deleterious health outcomes. In particular, there is evidence from clinical treatment samples and criminal justice populations that methamphetamine use is associated with depression, however this association has yet to be investigated in a nationally representative sample. Given that young adults are the group most prone to methamphetamine use, this study used a total of 8,688 respondents from Waves III (2001-02; ages 18-28) and IV (2007-08; ages 24-34) of the National Study of Adolescent Health (Add Health) to examine whether methamphetamine use (past year use at Wave III) was associated with depression, as measured by the Center for Epidemiologic Studies Depression Scale (CES-D). This study also evaluated whether gender, functional poverty status, polydrug use, and childhood maltreatment moderated the association between methamphetamine use and depression.

Logistic regressions were used to determine the odds ratios (OR) and 95% confidence intervals (95% CI) in unadjusted and adjusted analyses (controlling for gender, age, race/ethnicity, US region, functional poverty status, childhood maltreatment,

polydrug use, and depression at Wave III). Results indicated that in the general population, methamphetamine users have increased odds of becoming depressed (OR: 2.13, 95% CI: 1.38-3.27) and controlling for covariates, including Wave III depression, methamphetamine use independently predicted later depression (OR: 1.81, 95% CI: 1.12-2.92). None of the potential moderator variables tested had an effect on the association. These findings indicate that longitudinally, methamphetamine users are at an increased risk for depression, regardless of other factors and perhaps drug prevention and treatment programs for methamphetamine use should focus more on decreasing depression in this population. This study provides a broader understanding of the relationship between methamphetamine use and depression in a nationally representative sample, though further investigation into potential mediators and moderators is warranted.

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SECONDARY ANALYSIS

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Thesis submitted to the Faculty of the Graduate School of the  
University of Maryland, College Park, in partial fulfillment  
of the requirements for the degree of  
Master of Public Health  
2012

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## Acknowledgements

I would like to acknowledge my committee members, all exceptional researchers who supported me and guided me through the experience of completing my thesis. I would like to thank Dr. Sharon Desmond, my advisor, for the ongoing feedback and discussion, and helping me think through issues in directing this thesis. I am grateful to Dr. Amanda Berger for sharing her expertise on study design and data analyses techniques. Without her teaching and patience, I would have been unable to complete this thesis. I appreciate the advice and input provided by Dr. Kerry Green, especially in conceptualizing this project and understanding the analyses.

I would also like to thank Dr. Maria Khan, as it was through her mentorship and support that I began working with the National Longitudinal Study of Adolescent Health (Add Health), and developed an interest in working with population data. I would also like to acknowledge the Maryland Population Research Center for providing access to the data and assistance when needed.

This research used data from Add Health, a program project directed by Kathleen Mullan Harris and designed by J. Richard Udry, Peter S. Bearman, and Kathleen Mullan Harris at the University of North Carolina at Chapel Hill, and funded by grant P01-HD31921 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, with cooperative funding from 23 other federal agencies and foundations. Special acknowledgment is due Ronald R. Rindfuss and Barbara Entwisle for assistance in the original design. Information on how to obtain the Add Health data files is available on the Add Health website (<http://www.cpc.unc.edu/addhealth>). No direct support was received from grant P01-HD31921 for this analysis.

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## CHAPTER 1: INTRODUCTION

Methamphetamine is a highly addictive psychostimulant associated with significant physical, psychological and social consequences consisting of chronic illness and physical health problems (Gonzales, Mooney & Rawson, 2010); impaired cognitive functioning (Henry, Minassian & Perry, 2010; Meredith, Jaffe, Ang-Lee & Saxon, 2005; Scott, Woods, Matt, Meyer, Heaton et al., 2007; Simon, Domier, Sim, Richardson, Rawson, et al., 2002); risky sexual behaviors, such as increased sexual activity and inconsistent condom use (Darke, Kaye, McKetin & Duflou, 2008; Degenhardt, Coffey, Moran, Carlin & Patton, 2007; Molitor, Ruiz, Flynn, Mikanda, Sun, et al., 1999; Semple, Patterson & Grant, 2004; Zule, Costenbader, Meyer & Wechsberg, 2007); and psychiatric consequences, including psychosis, anxiety disorders, depression and suicide (Darke et al., 2008; Dyer & Cruickshank, 2005; Glasner-Edwards et al., 2008; Kalechstein et al., 2000; Marshall & Werb, 2010; Meredith, Jaffe, Ang-Lee, & Saxon, 2005; Salo, et al., 2011; Shoptaw et al., 2003; Zweben et al., 2004).

Specifically, depression is the most common psychiatric disorder associated with methamphetamine use (Glasner-Edwards et al., 2008; Nakama et al., 2008; Semple, Zians, Strathdee & Patterson, 2007; Sutcliffe et al., 2009; Zweben et al., 2004). Rates can reach as high as 68% of female and 50% of male methamphetamine users (Zweben et al., 2004). Depression, alone, is a significant public health issue, but for substance users, the effects can be especially dire; it has been linked to early treatment dropout (Curran, Kirchner, Worley, Rookey & Booth, 2002) and poorer outcomes overall (e.g., relapse) (McLellan, Luborsky, Woody, O'Brien & Druley, 1983).

## **Statement of the Problem**

Although the association between methamphetamine use and depression is well established, much of the research involves populations in treatment or in a criminal justice setting. It has been suggested that prevalence estimates obtained from populations in treatment may not accurately represent levels of depression among methamphetamine users who are not in treatment (Semple, Patterson & Grant, 2005). Further, it is necessary to study this relationship in the general population (as opposed to treatment or criminal justice populations) in order to truly identify the potential impact of methamphetamine use on depression. Given the negative health consequences of both methamphetamine use and depression, it is important to understand the longitudinal association between methamphetamine use and depression and to determine to what degree other variables may effect this association. Lastly, methamphetamine use generally is initiated in young adulthood (mean age of first use is 19.3 years) (SAMHSA, 2010), and young adults (ages 18-26) are the group most prone to use (SAMHSA, 2006) therefore it is important to examine this issue in an appropriate sample of young adults.

## **Significance of the Study**

The purpose of the current study was to examine the longitudinal association between methamphetamine use and depression. Specifically, data collected at Wave III (ages 18 to 28) and Wave IV (ages 24 to 34) from The National Study of Adolescent Health (Add Health), a nationally representative longitudinal survey, was analyzed to investigate whether methamphetamine use (past year use at Wave III, representing young adulthood) is associated with depression six years later, as measured by the Center for Epidemiologic Studies Depression Scale (CES-D). Logistic regression was used to

determine the odds ratios (ORs) and 95% confidence intervals (95% CIs) in unadjusted and adjusted analyses (controlling for gender, age, race/ethnicity, US region, functional poverty status, childhood maltreatment, polydrug use, and Wave III depression). An interaction term was created and added to the model to test modification of effect by gender, functional poverty status, childhood maltreatment, and polydrug use.

Examining factors that may affect the relationship between methamphetamine use and depression will likely provide a clearer understanding and enhance our ability to develop and deliver targeted interventions for both prevention and treatment purposes.

### **Research Questions**

This study used Waves III (2001-02; ages 18 to 28) and IV (2007-08; ages 24 to 34) of Add Health to examine the following research questions:

1. *What is the longitudinal association between methamphetamine use at Wave III (2001-02) and depression at Wave IV (2007-08)?*
2. *Is the relationship between methamphetamine use (at Wave III) and depression (at Wave IV) moderated by gender, functional poverty status, childhood maltreatment, or polydrug use?*

### **Definition of Terms**

The following are definitions of key terms that appear throughout the text.

- *Add Health* - The National Longitudinal Study of Adolescent Health (Add Health) is a longitudinal study of a nationally representative sample of adolescents in the United States.

- *Child maltreatment* – Any act or failure to act, on the part of a parent or caregiver, that results in death, serious physical or emotional harm, sexual abuse, or exploitation (HHS, 2003).
- *Depression* – A medical illness characterized by physical and emotional symptoms that interfere with an individual’s ability to work, sleep, study, eat, and enjoy pleasurable activities (NIMH, 2011). The Add Health interview uses a modified 9-item version of the Center for Epidemiologic Studies Depression Scale (CES-D) to measure depression.
- *Methamphetamine* – A powerful, highly addictive central nervous system stimulant. In Add Health, participants are asked specifically about ‘crystal meth’ use. Crystal meth is a highly pure, illicitly produced form of methamphetamine that can be smoked, snorted, injected, or taken orally. Until 2006, the National Survey on Drug Use and Health (NSDUH; SAMHSA, 2010) used the general term “methamphetamine” rather than crystal meth specifically, and questions pertaining to use were asked as part of the module on nonmedical use of prescription-type drugs (which was appropriate back when diverted pharmaceuticals were the primary type of methamphetamine used).Rutkowski and Maxwell (2009) believe that the Add Health designation of “crystal meth” produces a more accurate snapshot for the prevalence of use because it captures illicitly produced methamphetamine (Rutkowski & Maxwell, 2009).
- *Polydrug use* – The use of more than one illicit substance (e.g. marijuana, cocaine, methamphetamine) within a specified period of time. A broad definition may consider entire life history of substance use, whereas a more narrow definition may focus on

the past 12-months or 30-days. In this study, polydrug use is past year use of marijuana, cocaine, or heroin, and methamphetamine.

- *Substance abuse* – The use of a substance to the extent that harmful consequences occur as a result of repeated use and/or substance dependence (NIDA, 2009).
- *Substance dependence* - Substance dependence and addiction are synonymous terms. Addiction, as defined by the National Institute on Drug Abuse (NIDA), is a chronic disease characterized by compulsive drug seeking and abuse in spite of known adverse consequences, and by functional, sometimes long-lasting changes in the brain (NIDA, 2009).

## CHAPTER 2: LITERATURE REVIEW

### Description of Methamphetamine

Methamphetamine is a highly addictive, powerful central nervous system stimulant. As a methyl derivative of amphetamine, the chemical structure and effects of methamphetamine are similar to that of amphetamine, as they both increase stimulation of dopamine and norepinephrine receptors in the brain (Anglin, Burke, Perrochet, Stamper & Dawud- Nours, 2000). Similar to other amphetamine-type stimulants, methamphetamine is a controlled substance and a Schedule II class drug. The commonly used and street-acquired methamphetamine, typically found as white powder or translucent crystals, may be referred to as 'ice,' 'crank,' 'tina,' 'speed,' 'glass,' or 'crystal meth' (NIDA, 2006). Methamphetamine can be smoked; snorted; or consumed orally, rectally, and intravenously, though smoking methamphetamine is the most common route of administration (NIDA, 2006). The route of administration and dose ingested are directly related to the intensity, onset, and length of effects, and both smoking and injection use are more likely to lead to dependence (McKetin, Kelly & McLaren, 2006).

Unlike imported drugs, such as cocaine and heroin, illicit methamphetamine is easy to manufacture using pharmaceutical, agricultural, and industrial products that are publicly available (Greene, Kerr & Braitberg, 2008). As a result, methamphetamine production often occurs in clandestine home laboratories (sometimes referred to as "meth labs") that are typically operated by methamphetamine abusers (Hunt, 2006). These laboratories are often found in residential homes and present additional public health risks, as many chemicals used in the production and resulting by-products of "cooking" methamphetamine are hazardous and toxic, and thus dangerous to the community

surrounding the lab and any individuals in the home (OCOPS, 2002). For every pound of methamphetamine manufactured in a clandestine meth lab, an estimated five to six pounds of hazardous waste are produced (Hunt, Kuck & Truitt, 2006).

Methamphetamine was first synthesized at the end of the 19<sup>th</sup> century by a Japanese pharmacologist, but it was not widely used until World War II, when Germany, Japan and the United States (US) supplied the drug for military use as it increased performance and endurance (Anglin, Burke, Perrochet, Stamper & Dawud- Nours, 2000). In the United States, the illicit market mainly consisted of diverted pharmaceuticals (misused prescription medication that was prescribed for the treatment of asthma) until the illicit production of methamphetamine emerged in the early 1960's and use spread along the Pacific Coast as Bay Area motorcycle gangs controlled manufacturing and distribution (Anglin, et al., 2000). By 1980, simpler methods for home production were developed using an ephedrine-based reduction method (Anglin, et al., 2000) and at the same time, large quantities of a highly pure, crystallized form of methamphetamine ("crystal meth") were smuggled into California from Mexico and distributed throughout the Southwestern and Midwestern states (Anglin, et al., 2000).

During this period, methamphetamine use increased in Hawaii, as 'ice' began to be imported from Southeast Asia and the Philippines, and spread throughout the United States (Gonzales, Mooney & Rawson, 2010). Given the availability of the precursor chemicals, such as pseudoephedrine, used to produce methamphetamine and the relative ease of manufacture, in 2005, the US federal government enacted the Combat Methamphetamine Epidemic Act (CMEA), which limited the sale of products containing pseudoephedrine (e.g. over-the-counter cold medicine, Sudafed) (ONDCP, 2010).

Although there is evidence of a decrease in methamphetamine use since the passage of CMEA, methamphetamine producers have found ways around CMEA and the number of methamphetamine lab incidents involving law enforcement have increased; there were 966 lab seizures nationwide in March 2009 compared to 596 incidents in March 2007 (ONDCP, 2010).

### **Effects of Methamphetamine Use**

Similar to other psychostimulants (e.g. cocaine), the immediate physiological response of methamphetamine intoxication includes increased alertness, physical activity, respiration, heart rate and blood pressure, and decreased appetite (NIDA, 2006). The “high” creates an elevated positive mood and feeling of euphoria that can last between eight-12 hours due to the 12-hour half-life of methamphetamine (Cho, Melega, Kuczenski, & Segal, 2001). In addition to intense euphoria, other positive reinforcing attributes of methamphetamine use include increased energy and alertness, heightened mental capacity, enhanced libido and decreased anxiety (Meredith et al., 2005). However, there are many negative health outcomes associated with repeated methamphetamine use, including insomnia, hyperthermia, stroke, stomach cramps, cardiac arrhythmia, and seizures (NIDA, 2009). Methamphetamine associated fatalities are most commonly attributed to pulmonary congestion, cerebrovascular hemorrhage (as a result of hypertension), acute cardiac failure or hyperpyrexia, though there is evidence that a significant number of deaths (possibly a greater proportion than the latter) arise from accidents, suicides and homicides resulting from behavioral and psychological disturbances from methamphetamine intoxication (Cruickshank & Dyer, 2009).

Withdrawal from methamphetamine, often referred to as “the crash,” typically



results in more psychological discomfort than physical symptoms and usually includes depressed mood with severe dysphoria, anxiety, irritability, hypersomnia, fatigue and intense craving for the drug (Meredith, Jaffe, Ang-Lee & Saxon, 2005). The severity of these symptoms seems to be related to the frequency and intensity of use (Meredith et al, 2005). Methamphetamine dependence is more strongly associated with injection use and smoking the drug, and it is hypothesized that many of the negative health consequences, such as those listed above, result from dependence due to long-term, frequent use (McKetin, Kelly & McLaren, 2006). In addition to frequency of use, potency of the drug may increase the likelihood of dependence (Darke, Kaye, McKetin & Dufrou, 2008).

Repeated methamphetamine use is also associated with decreased daily functioning, indicated by poor performance in a variety of areas, including cognitive tasks related to comprehension and planning, communication skills, and activities such as managing medication or participating in financial transactions (Henry, Minassian & Perry, 2010). Noninvasive brain imaging studies show that long-term methamphetamine abuse or dependence is linked to structural brain alterations and metabolic and neurotransmitter irregularities (Scott et al., 2007), which may underlie the observed association between methamphetamine use and impaired cognitive function and problems regulating emotions. Stimulants and other illicit drugs have previously been linked to neurocognitive changes; however, methamphetamine use is linked to distinctive impairments that endure during protracted abstinence (e.g. several months or more) (Meredith et al., 2005).

In addition, compared to individuals who abuse other stimulants and illicit drugs, there is evidence that methamphetamine users develop different cognitive impairments

(Simon et al., 2002). Simon and colleagues (2002) conducted a study comparing neurocognitive performance between active methamphetamine users (n=40), cocaine users (n=40) and non-psychostimulant using controls (n=80), and found that though both methamphetamine and cocaine users have impairments in verbal memory, methamphetamine users also showed impairment on tasks measuring perceptual speed and information manipulation, suggesting they may have difficulty organizing information from more than one source and trouble switching points of view (Simon et al., 2002). Such deficits may translate to poor comprehension and ultimately affect one's ability to participate in substance abuse treatment, understand legal proceedings, and follow regimens set by healthcare providers.

Methamphetamine users often consume other substances (polydrug use), including alcohol, marijuana, other psychostimulants, and heroin, and though polydrug use is associated with poor clinical outcomes, there are specific harms that result from concomitant use of methamphetamine and other substances (Darke, Kaye, McKetin & Dufrou, 2008). When methamphetamine is combined with other substances, such as alcohol, opiates, or cocaine, the toxicity of methamphetamine increases (Albertson, Derlet & Van Hoozen, 1999). Given the physiologic effects (e.g., increased heart rate and blood pressure), concomitant use of methamphetamine with other substances may increase risk of cardiac failure and death (Albertson, Derlet & Van Hoozen, 1999).

There is evidence for additional negative health outcomes due to methamphetamine use and increased participation in unsafe sexual behaviors (e.g., multiple partners, unprotected intercourse) and other risky behaviors (i.e., sharing needles) (Darke et al., 2008; Degenhardt, Mathers, Guarinieri, Panda, et al., 2010;

Molitor et al., 1999; NIDA 2009; Semple, Patterson & Grant, 2004; Zule, Costenbader, Meyer & Wechsberg, 2007), increasing the likelihood of exposure to and transmission of Hepatitis C and human immunodeficiency virus (HIV). Research conducted by Semple, Patterson, and Grant (2004) compared the sexual behaviors of heterosexual methamphetamine users (n=181) recruited through community outreach programs to national data and found that on average, methamphetamine users were more sexually active, as they reported having vaginal intercourse 19.8 times per month (compared to the national average of 6.5 times per month) and participants averaged 11.2 sexual partners over 2-months, compared to the national average of 1.3 per year among heterosexual non-drug users. In addition, the rates of unprotected intercourse in a 2-month period (whether it was vaginal, anal, or oral sex) were also high in this population (mean number of times = 29.6, 13.1, 52.1, respectively), suggesting that methamphetamine users are at increased risk for contracting HIV and other sexually transmitted infections due to their increased sexual activity and high rates of unprotected sex (Semple, Patterson & Grant, 2004).

Similarly, Molitor and colleagues (1998) found that individuals who use methamphetamine are at greater risk for HIV-infection because they reported more sexual partners than non-methamphetamine users, and methamphetamine use was independently related to decreased condom use during intercourse (vaginal and anal), prostitution, and sex with injection drug users (Molitor, Truax, Ruiz, & Sun, 1998). Other research examining the relationship between methamphetamine use and HIV has found that HIV positive methamphetamine users have increased cognitive impairment and neuronal injury compared to HIV-positive non-users (Chang, Ernst, Speck, & Grob,

2005). In general, methamphetamine use is associated with increased rates of HIV, in part because of risky sexual behaviors, but also because methamphetamine use causes physiological changes that facilitate the transmission of HIV and conversion to acquired immunodeficiency syndrome (AIDS) (Venios & Kelly, 2010). As a vasoconstrictor, methamphetamine causes mucus membranes to dry, leading to the formation of genital ulcers, which increases the risk of transmission (Dickerson, Johnston, Delea, White, & Andrews, 1996).

In addition to the consequences of use on physical health, methamphetamine is associated with psychiatric disorders including psychosis, anxiety, and depression (Darke, et al., 2008; Kalechstein et al., 2000; Marshall & Werb, 2010; Meredith et al., 2005; Salo, Flower, Kielsein, et al., 2011; Zweben, et al., 2004). Studies have shown that approximately half of methamphetamine users have been diagnosed with a psychiatric disorder (e.g., major depressive disorder, bipolar disorder) as measured by the DSM-IV (Dyer & Cruickshank, 2005; Glasner-Edwards, Mooney, Marinelli-Casey et al., 2010; Shoptaw, et al., 2003), which is nearly double the national prevalence of diagnosed disorders (NIMH, 2011).

Methamphetamine induced psychosis is typically transient, involving hallucinations and delusions (with persecutory themes) and may be accompanied by emotional instability, agitation, and hostility (Darke, et al., 2008). In a study by McKetin and colleagues (2006), methamphetamine users (n=309) were interviewed to assess the prevalence of psychosis within this population. Findings show that after excluding participants with a history of schizophrenia or other psychotic disorders, 18% of participants screened positive for clinically significant psychotic symptoms (McKetin,

McLaren, Lubman & Hides, 2006). In a more recent study among methamphetamine users (n=526) at three years following substance abuse treatment, 13% of participants met criteria for a lifetime psychotic disorder (Glasner-Edwards, et al., 2010).

Depression is the most common comorbid psychiatric disorder associated with methamphetamine use (Glasner-Edwards, et al., 2009; Nakama, et al., 2008; Semple, et al., 2007; Sutcliffe, et al., 2009; Zweben, et al., 2004). In substance abuse treatment populations, there is evidence that methamphetamine users have higher rates of depressive symptoms, that persist longer, compared to cocaine users (Rawson, et al., 2002). In a study conducted with a large sample of methamphetamine users (n=1,061) in outpatient treatment, Zweben and colleagues (2004) found high levels of depression among both women (68%) and men (50%), and 27% of the entire sample reported a suicide attempt in their lifetime. In another study by Kalechstein and colleagues (2000), a sample of arrestees (n=1,580) was surveyed to assess the association between methamphetamine dependence and psychiatric symptoms. Findings showed that after controlling for demographic characteristics and dependence on other drugs in the 12-months prior to the assessment, individuals dependent on methamphetamine were more likely to report symptoms of depression and thoughts of suicide, compared to individuals not reporting methamphetamine dependence (Kalechstein et al., 2000).

### **Explanations for the Association Between Methamphetamine Use and Depression**

As previously noted, there is an established link between substance use and depression; however, there is still much debate over the etiology of depression among substance users. Early studies using animals to demonstrate the effect of methamphetamine use on the brain have shown that use induces profound and enduring

damage to dopamine cells (Preston, Wagner, Schuster & Seiden, 1985). More recent research employing neuroimaging techniques with humans has shown that chronic methamphetamine users exhibit reductions in dopamine neurotransmission (Volkow et al., 2001; Wang et al., 2004), which may be related to depression and anhedonia (Dunlop & Nemeroff, 2007). Dopamine appears to play a role in both methamphetamine use and depression, making the relationship particularly difficult to tease out. Another potential explanation for the observed neurobiological changes is that there are common factors, either genetic or environmental, that precede the onset and/or persistence of both substance use and depression (Kessler, 2004).

### **Ecological Model**

To examine the relationship between methamphetamine use and depression and to identify and evaluate factors that may affect this relationship, this study used an ecological perspective, which is a model that allows for consideration of the multipart interplay between the individual and their environment. Specifically, the ecological model proposed by Bronfenbrenner (1977) places the individual in the center of several concentric circles, each representing a different level of interaction: microsystem (individual level), mesosystem (familial level), exosystem (community level) and macrosystem (societal level).

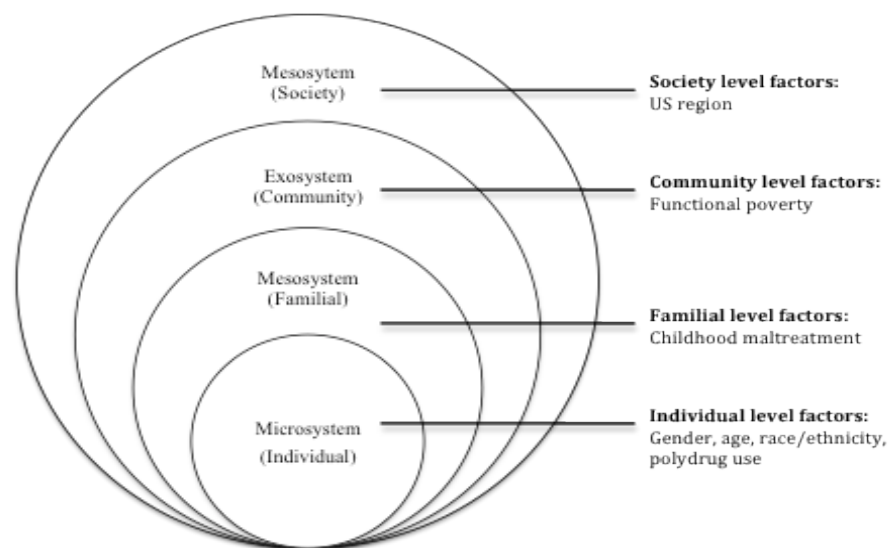
According to Bronfenbrenner (1977), these system levels influence human development within a broad, ecological framework and the level of influence of different factors on the individual is represented by the proximity of each circle to the individual, representing direct or indirect factors. Application of an ecological model to understand

the association between methamphetamine use and depression allows for consideration of several variables at different levels of influence and how they may affect the association.

### **Ecological Model and Moderators**

As previously noted, depression is common among methamphetamine users. However, to the author's knowledge, there is no research establishing the temporal order of methamphetamine use and depression in a general population sample. Further, not all methamphetamine users experience depression and there is little research identifying other factors that may play a role in this relationship. Using the ecological model as a framework for choosing variables to examine, specific factors identified at each level of the model may act as modifiers of the relationship between methamphetamine use and depression (Figure 1).

*Figure 1. Adaptation of the Ecological Model: Potential Moderators of the Relationship Between Methamphetamine Use and Depression, including Covariates*



According to Baron and Kenny (1986), moderation occurs when the causal relationship between two variables differs as a function of the moderator. A moderator specifies on whom or under what conditions the independent variable will operate to produce the dependent variable (Baron & Kenny, 1986). Beginning at the micro level (i.e. individual), factors such as gender, race/ethnicity, and age may play a role in the relationship between methamphetamine use and depression.

The microsystem consists of individual level factors that generate a social identity, including gender and polydrug use. Previous studies suggest that a gender difference exists in depression levels among methamphetamine users, as higher rates of depression are observed among female methamphetamine users (Glasner-Edwards, et al., 2008; Zweban, et al., 2004). However, these findings may represent the general trend of higher rates of depression among women, compared to men, in the general population (Kessler, et al., 2005). Given the ambiguity, further exploration into how gender affects the association between methamphetamine use and depression is warranted.

Polydrug use is common among substance users (Booth, Leukefeld, Falck, Wang, & Carlson, 2006; Byqvist, 2006; Darke, et al., 2008), particularly methamphetamine users (Brecht, Greenwell & Anglin, 2005). Further, polydrug use is associated with depression (Roiser & Sahakian, 2004). McKetin and colleagues (2011) found that among methamphetamine users in substance abuse treatment, concurrent polydrug use (in particular, use of cannabis and benzodiazepines) was significantly associated with depression (McKetin, Lubman, Lee, Ross & Slade, 2011). Given these findings and the evidence that methamphetamine users are likely to use multiple substances concurrently,



the relationship between methamphetamine use and depression may be moderated by polydrug use.

The mesosystem (familial level) consists of the interrelations in major settings that contain the person at specific period of development and encompasses interactions between the individual and family, peer group and other caregivers (Bronfenbrenner, 1977). Childhood maltreatment, specifically physical and sexual abuse, is a strong and consistent predictor of depression (Bifulco, Brown & Adler, 1991; Fletcher, 2009; Molnar, Buka & Kessler, 2001) and is highly correlated with adult substance use (Dube et al., 2003; Kendall-Tackett, 2002; Nelson et al., 2002; Silverman, Reinherz, & Giaconia, 1996). Brown and colleagues (1999) conducted a prospective cohort study with a sample of 776 individuals. After controlling for contextual factors, including family environment and parent and child characteristics, young adults who experienced childhood maltreatment were nearly four times more likely to be depressed compared to young adults with no history of childhood maltreatment (Brown, Cohen, Johnson & Smailes, 1999). In considering the association between methamphetamine use and depression, childhood maltreatment may be a moderator.

The exosystem (community level), an extension of the mesosystem, contains both formal and informal social structures that do not necessarily contain the individual, but rather impinge on the immediate settings of that person, ultimately influencing, delimiting, or even determining what occurs there (Bronfenbrenner, 1977). Functional poverty, an exosystem level variable, is associated with increased odds of methamphetamine use (Iritani, et al., 2007) and there is also evidence that it is associated with an increased risk of depression (Riolo, Nguyen, Greden & King, 2005).

In addition, there are several variables that should be considered covariates as previous research has identified each as a risk factor associated with methamphetamine use or depression. For example, age is a well-established risk factor associated with depression, with higher rates observed among young adults (Blazer, Kessler, McGonagle, & Swartz, 1994) and Whites, compared to other minorities, are more likely to be depressed (Kessler, et al., 1997; Riolo, Nguyen, Greden & King, 2005). Lastly, people living in the western United States and the South are more likely to be methamphetamine users, compared to people living in the Midwest or Northeast (Iritani, et al., 2007).

## **CHAPTER 3: METHODS**

### **Description of the Data**

The National Longitudinal Study of Adolescent Health is a prospective cohort study of a nationally-representative sample designed to evaluate how social environments and behaviors in adolescence are associated with health and other outcomes into adulthood (Harris, et al., 2009). The Add Health project was directed by Kathleen Mullan Harris and designed by J. Richard Udry, Peter S. Bearman, and Kathleen Mullan Harris at the University of North Carolina at Chapel Hill, and funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, with cooperative funding from 23 other federal agencies and foundations. Access to Add Health restricted-use data is available by contractual agreement with the Inter-University Consortium for Political and Social Research (ICPSR) through the Data Sharing for Demographic Research (DSDR) archive.

### **Sampling Procedures**

As the largest, most comprehensive, longitudinal study of adolescents, Add Health began in 1994, with the identification of a sample consisting of 80 high schools and 52 middle schools with unequal probability of selection (Harris, et al., 2009). For the school sample, high school eligibility was determined by having an 11<sup>th</sup> grade and an enrollment of at least thirty students. The schools were stratified by region, school type (public, private, parochial), urbanity, ethnic mix, and size. One feeder school (typically a middle school, as eligibility was determined by inclusion of a 7<sup>th</sup> grade) for each high school was recruited, unless the high school included 7<sup>th</sup> grade. More than 70 percent of schools identified agreed to participate in the study, which resulted in a total of 132

schools associated with 80 different communities. Schools that declined were replaced with a school in the same stratum.

From September 1994 until April 1995 (Wave I), in-school questionnaires were administered within a single 45- to 60-minute class period to more than 90,000 students. Survey questions included measurement of future expectations, school activities, friendship networks, and various health conditions. Using school enrollment data as the sampling frame for the in-home interview, students were stratified in each school by grade and sex, and about 17 students from each strata (a total of approximately 200 adolescents from each pair of schools) were randomly chosen to form a core sample for home surveys of 12,105 students (participation in the in-school survey did not affect eligibility for inclusion in the in-home interview sample) (Harris, et al., 2009).

Supplemental samples were created using responses to the in-school survey and participants were selected based on ethnicity (Cuban, Puerto Rican, and Chinese), genetic relatedness to siblings (e.g. twins, full siblings, half siblings), and adoption status and disability. Black adolescents with highly-educated parents were also oversampled (Harris, et al., 2009). The core sample and additional special samples yielded a sample size of 20,745 adolescents for the Wave I in-home interview, and this sample is the basis for all subsequent waves of data collection (Harris, et al., 2009).

### **Survey Design**

The in-home interview, administered in 1994-95, included sections on family and peer relationships, risk-taking behaviors (including substance use, delinquency, and sexual-risk behaviors), and general health. The in-home survey also included a 30-minute parent interview (typically completed by the resident mother) that asked questions about

health conditions, relationships, employment, income, education, parent-teen communication and interaction, and neighborhood characteristics; approximately 85% of the parents of participants completed the parental supplement (Harris, et al., 2009). One year later, in 1996, the Wave II in-home interview was conducted with the 14,738 adolescents from the original sample of 20,745 participants (Harris, et al., 2009).

In 2001-02, respondents (now ages 18-28) were contacted, and 76% (N=15,197) of the original sample completed a follow-up survey (Wave III). Data were collected regarding health and related behaviors, access and use of healthcare services, sexual behavior, mental health, substance use, delinquency and violence. The Wave III in-home questionnaire also included questions about family relationships, mentoring relationships, personal income, civic participation, criminal justice involvement and religion and spirituality. In addition, retrospective questions were asked about childhood maltreatment prior to grade six (including neglect, physical, and sexual abuse).

For the most recent follow-up (Wave IV, conducted between 2007-08 with participants now ages 24-34) the Add Health team located 92.5% of the original sample members and completed interviews with approximately 80% (n=15,709). In Wave IV, data was collected on sections included in previous waves, to maintain the longitudinal design of the survey. Expanded questions on substance use, including criteria for abuse and dependence, were added to Wave IV, in addition to several other domains, such as measure of personality dimensions, interpersonal and occupational stressors, and work and family responsibilities.

All in-home interviews at each wave were completed on a laptop computer (supplied by the Add Health interviewer) and conducted in respondent's home (though

this was not a requirement, and Add Health interviewers made arrangements with a handful of participants to complete the interview at a location that better accommodated the participant's schedule). Less sensitive questionnaire sections were completed with the assistance of an interviewer (computer-assisted personal interview), and the more sensitive sections were administered using audio-computer assisted self interview (ACASI) technology. ACASI is an interview technique that uses a laptop computer and headphones to provide a spoken recording of each question as it is presented on the screen. Responses to questions are entered directly into the computer by the participant. This format provides more privacy than the standard questionnaire format and helps reduce self-report bias for sensitive behaviors (e.g. substance use and high-risk sexual behaviors).

### **Analytic Sample**

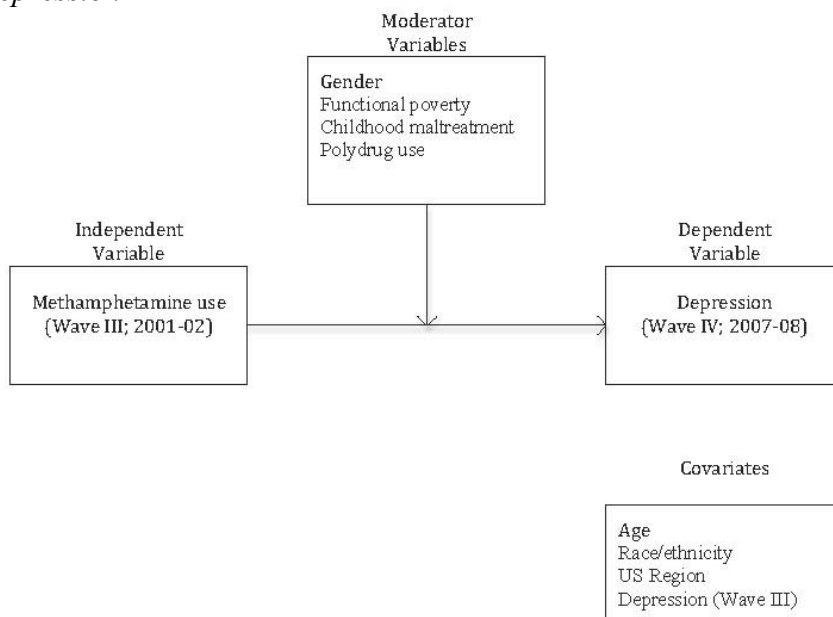
This study examined young adult past year methamphetamine use (independent variable) at Wave III (2001-02) and later depression (dependent variable) at Wave IV (2007-08). Combining these two waves, the initial sample size started with N=17,864 and was reduced to n=13,034 after all unmatched cases were dropped. To examine longitudinal associations, only respondents with valid weights, cluster and strata values were included in the sample (n=9,421), and only respondents with non-missing responses for the independent and dependent variables were retained in the analytic sample (n=9,309). T-tests revealed that those with missing values and those with no missing values were not significantly different on key variables, such as gender, race/ethnicity, and functional poverty. For all variables that were tested as moderators or used as covariates, as is standard practice, if less than 5% of the data were missing, the missing

values were replaced with the mode for categorical variables (gender, race/ethnicity, US region, polydrug use, and functional poverty) and the mean for continuous variables (age). Childhood maltreatment had 7% missing and therefore, these cases were dropped from the analytic sample. T-tests revealed that there were no significant differences on key variables between those included in the analytic sample and those who were dropped, except that those missing were more likely to be male ( $p < 0.05$ ). As a result, the final analytic sample used to examine the associations between methamphetamine use and depression for all logistic regressions in this study was  $n = 8,688$ .

### Variables

In the current study, the independent variable, methamphetamine use, was measured by past year crystal meth use; the dependent variable, depression, was based on CES-D scores; four variables were tested as potential moderators (gender, functional poverty, polydrug use, and childhood maltreatment), and there were four additional covariates (age, race/ethnicity, US region, and Wave III depression) (Figure 2).

*Figure 2. Conceptual Model: The Relationship Between Methamphetamine Use and Depression*



*Independent Variable: Methamphetamine Use (Wave III)*

Past Year Methamphetamine Use. Respondents were asked, “*Have you used crystal meth in the past year?*” Those who reported use in the past year were considered past year crystal methamphetamine users and responses were coded dichotomously (“yes” versus “no,” the referent).

*Dependent Variable: Depression (Wave IV)*

Depression. To measure depression, the Add Health interview contains a 9-item depressive symptoms scale modified from the 20-item Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977; Santor & Coyne, 1997). Respondents were asked to indicate the frequency with which they experienced certain feelings in the past seven days. The feelings statements included: “*You were bothered by things that don’t usually bother you. You could not shake off the blues, even with help from your family and friends. You felt you were just as good as other people. You had trouble keeping your mind on what you were doing. You felt depressed. You felt that you were too tired to do things. You felt happy. You enjoyed life. You felt sad.*” Response options were 0 (never or rarely), 1 (some or little of the time), 2 (occasionally or a moderate amount of time), and 3 (most of the time or all the time) and were summed to produce a score between 0 and 27. Following the methods of previous researchers, a cut-off score was used to determine whether a respondent is “depressed” based on the top quintile of the distribution of CES-D scores as determined in initial analyses (Cesur, Sabia, & Tekin, 2011; Goodman & Capitman, 2000; Tekin, Erdal & Markowitz, 2008) and coded dichotomously (“depressed” versus “not depressed,” the referent). In this sample a score of 13 was used to determine the cut-off for the top quintile of scores. Therefore, a score of 13 or greater



was coded as “depressed” and a score of 12 or less was coded as “not depressed,” the referent.

*Moderator Variables (Wave III)*

Gender. Gender was based on respondent self-report at Wave III. Responses were coded dichotomously (“male” or “female,” the referent).

Functional Poverty Status. At Wave III, respondents were asked, “*In the past 12 months, was there a time when you didn’t pay the full amount of the rent or mortgage because you didn’t have enough money?*” and “*In the past 12 months, was there a time when you didn’t pay the full amount of a gas, electricity, or oil bill?*” Responses were coded dichotomously (“yes” versus “no,” the referent) and low functional poverty status was defined by an affirmative response to either question.

Polydrug Use. Respondents were asked, “*In the past year have you used marijuana? Any kind of cocaine – including crack, freebase or powder? Any other types of illegal drugs, such as LSD, PCP, ecstasy, mushrooms, inhalants, ice, heroin, or prescription medicines not prescribed for you?*” An affirmative response for two or more of the substance use questions was coded as 1 (“yes”) and responses of one or zero were coded 0 (“no”).

History of Childhood Maltreatment. At Wave III, respondents were asked retrospectively about childhood maltreatment that occurred by the sixth grade. Neglect was measured by asking, “*How often had your parents or other adult caregivers left you home alone when an adult should have been with you?*” and “*How often had your parents or other adult caregivers not taken care of your basic needs, such as keeping you clean or providing food or clothing?*” Physical abuse was measured by asking

respondents, “*How often had your parents or other adult caregivers slapped, hit or kicked you?*” Based on the methods of Currie and Tekin (2006) responses were coded dichotomously (“yes” versus “no,” the referent) if the respondent reports 10 or more occurrences of neglect and/or physical abuse. Sexual abuse was measured using the following question, “*How often had one of your parents or other adult caregivers touched you in a sexual way, forced you to touch him or her in a sexual way, or forced you to have sexual relations?*” Responses to this item were coded “yes” if the respondent reports any instance of sexual abuse, versus “no” (none), the referent. Together, these two items were combined to generate a single variable called “childhood maltreatment” and coded dichotomously, “yes” vs. “no,” the referent.

#### *Covariates (Wave III)*

Age. Age, a continuous variable, was measured at Wave III based on self-report.

Race/Ethnicity. Race/ethnicity is a nominal variable that was categorized based on respondent self-report. Respondents were coded as either “White” (the referent), “African American,” “Latino,” “Native American,” or “Asian American.”

US Region. US region is a categorical variable. Add Health assigns the corresponding US census region (“West,” “South,” “Midwest” or “Northeast,” the referent) based on respondents’ address of residence.

Depression. Wave III depression was also measured using the CES-D and the same methods as Wave IV depression as described above. However, based on the distribution of the responses, a cut-off score of 9 was used to represent the top quintile or “depressed” respondents. Those with a score of 8 or below were coded as “not depressed,” the referent.

## Data Analysis

All analyses were conducted using Stata version 11.0 (Stata Corp., College Station, TX, USA). In Stata, survey commands were used to account for stratification and clustering. Unequal selection probability were used, and appropriate weights were applied to ensure a nationally-representative sample. Descriptive statistics were conducted for all study variables. For continuous variables (e.g., age), means and confidence intervals were reported. Categorical variables (e.g., gender, race/ethnicity, functional poverty, etc.) were reported using weighted frequencies.

*Research Question 1a: What is the longitudinal association between methamphetamine use at Wave III (2001-02) and depression at Wave IV (2007-08)?*

*Research Question 1b: What is the longitudinal association between methamphetamine use at Wave III (2001-02) and depression at Wave IV (2007-08), controlling for depression at Wave III?*

Logistic regressions were used to estimate the unadjusted odds ratios and 95% confidence intervals for the associations between methamphetamine use and depression. Adjusted ORs and 95% CIs (controlling for gender, age, race/ethnicity, US region, functional poverty, childhood maltreatment, polydrug use, and Wave III depression) for the associations between methamphetamine use and depression were examined and reported.

*Research Question 2: Is the relationship between methamphetamine use (at Wave III) and depression (at Wave IV) moderated by gender, functional poverty, childhood maltreatment, or polydrug use?*

To examine whether the association between methamphetamine use and depression differed by gender, functional poverty status, polydrug use, or childhood maltreatment, an interaction term was tested for significance ( $p < 0.05$ ). If the interaction term was significant then the variable was considered to be a moderator of the association.

## CHAPTER 4: RESULTS

### Population Sociodemographic Characteristics

A total of 8,688 individuals were included in the final analytic sample. Table 1 illustrates the sample characteristics on key variables. A little more than half of the respondents were female (51%). The majority of respondents were white (69%), African American (15%), or Latino (12%), and a small proportion were Asian American (3%) or Native American (<1%). At Wave III, the mean age of respondents was 21.6 years ( $SD=1.63$ ). The largest proportion of respondents resided in the South (39%) and nearly a third lived in the Midwest (32%); remaining respondents were from the West (17%) or Northeast (13%). Approximately 14% of the analytic sample met criteria for functional poverty. About 36% reported polydrug use, and nearly 18% had experienced childhood maltreatment.

### Sociodemographic Characteristics of Methamphetamine Users

In this study, 2.9% ( $n=243$ ) of the young adults (ages 18-28) interviewed at Wave III, reported past year methamphetamine use (Table 1). Methamphetamine users were twice as likely to be male (OR: 2.00, 95% CI: 1.35-2.97). Compared to Whites, only Native Americans had an increased risk of methamphetamine use (OR: 2.59, 95% CI: 1.07-6.29), however the confidence interval was wide and the elevated odds ratio may be a result of the small number of Native Americans in the sample ( $n=77$ ). Age was categorized into three groups, 18-20 years, 21-22 years, and 23-28 years based on distribution, and no age group was significantly more likely to use methamphetamine. Methamphetamine users were most likely to live in the West (OR: 4.06, 95% CI: 1.94-8.52) or South (OR: 2.19, 95% CI: 1.05-4.55), compared to the Midwest or Northeast.

*Table 1. Associations Between Respondent Characteristics and Methamphetamine Use among Young Adults (N=8,688) ages 18-28, in the United States (US)†*

	N=8,688	Weighted %	Weighted % of Past Year Meth Use (n=243)	Unadjusted Odds Ratios (95% Confidence Intervals)
<b>Gender</b>				
Female	4,829	51.0%	2.0%	Referent
Male	3,859	49.0%	3.9%	2.00 (1.35-2.97)
<b>Race</b>				
White	4,994	68.8%	3.6%	Referent
African American	1,778	15.2%	0.3%	0.08 (0.03-0.23)
Latino	1,317	12.0%	2.1%	0.57 (0.28-1.16)
Native American	77	0.7%	8.8%	2.59 (1.07-6.29)
Asian	522	3.3%	2.0%	0.54 (0.21-1.35)
<b>Age (Years)</b>				
Mean	21.6 (21.58-21.65)			
18-20	2,373	33.9%	3.0%	Referent
21-22	3,474	38.4%	3.2%	1.06 (0.69-1.64)
23-28	2,841	27.7%	2.3%	0.75 (0.45-1.24)
<b>Region</b>				
Northeast	1,059	13.2%	1.3%	Referent
Midwest	2,366	31.6%	2.6%	1.99 (0.96-4.13)
South	3,227	38.5%	2.8%	2.19 (1.05-4.55)
West	2,036	16.7%	5.1%	4.06 (1.94-8.52)
<b>Functional Poverty</b>				
No	7,513	86.5%	2.7%	Referent
Yes	1,175	13.5%	4.1%	1.55 (1.02-2.36)
<b>Polydrug Use</b>				
No	5,788	64.0%	0.1%	Referent
Yes	2,900	36.0%	7.8%	67.00 (28.66-156.63)
<b>Childhood Maltreatment</b>				
No	7,080	82.4%	2.2%	Referent
Yes	1,608	17.6%	6.1%	2.88 (2.11-3.92)

†Survey commands accounting for stratification, clustering, and unequal selection probabilities yielded nationally representative estimates.

Methamphetamine users were more likely to live in functional poverty (OR: 1.55, 95% CI: 1.02-2.36) compared to non-users, and were much more likely to use other illicit drugs (OR: 67.00, 95% CI: 28.66-156.63). Methamphetamine users were nearly three times more likely to experience childhood maltreatment compared to non-users (OR: 2.88, 95% CI: 2.11-3.92).

### **Associations Between Methamphetamine Use and Depression**

*Model 1.* Unadjusted analyses showed that Wave III methamphetamine use was associated with an increased risk of depression at Wave IV (OR: 2.13, 95% CI: 1.38-3.27) (Table 2, Model 1).

*Model 2.* Adjusted analyses (controlling for gender, age, race/ethnicity, US region, functional poverty, polydrug use, and childhood maltreatment) revealed that Wave III methamphetamine use was an independent predictor of Wave IV depression (AOR: 2.04, 95% CI: 1.29-3.21) (Table 2, Model 2).

Covariates. In this model, being African American, living in functional poverty, and experiencing childhood maltreatment were all variables associated with increased risk of depression at Wave IV.

*Model 3.* Adjusted analyses controlling for Wave III depression revealed that Wave III methamphetamine use was associated with an increased risk of depression at Wave IV (AOR: 1.78, 95% CI: 1.14-2.76) (Table 2, Model 3). Covariates. In this model, only Wave III depression was used as a covariate, and it was associated with more than five times the likelihood of Wave IV depression (Table 2, Model 3). *Model 4.* Adjusted analyses (controlling for Wave III depression, gender, age, race/ethnicity, US region, functional poverty, polydrug use, and childhood maltreatment) showed that Wave III

Table 2. Associations Between Methamphetamine Use and Depression Among Young Adults(N=8,688) in the US†

	Model 1	Model 2	Model 3	Model 4
<b>Exposure</b>				
Wave III Meth	2.13 (1.38-3.27)	2.04 (1.29-3.21)	1.78 (1.14-2.76)	1.81 (1.12-2.92)
<b>Covariates</b>				
Wave III Depression			5.30 (4.17-6.74)	4.69 (3.65-6.03)
Gender				
Female		Referent		Referent
Male		0.53 (0.41-0.68)		0.60 (0.47-0.77)
Age				
18-20		Referent		Referent
21-22		1.10 (0.84-1.44)		1.08 (0.83-1.41)
23-28		1.11 (0.84-1.48)		1.19 (0.89-1.59)
Race				
White		Referent		Referent
African American		1.80 (1.19-2.72)		1.64 (1.10-2.42)
Latino		0.99 (0.72-1.36)		0.83 (0.59-1.17)
Native American		1.31 (0.37-3.49)		1.15 (0.42-3.12)
Asian		0.81 (0.46-1.44)		0.73 (0.43-1.26)
US Region				
Northeast		Referent		Referent
Midwest		0.98 (0.55-1.73)		1.06 (0.61-1.84)
South		1.00 (0.53-1.89)		1.05 (0.57-1.93)
West		0.94 (0.52-1.69)		0.95 (0.53-1.67)
Functional Poverty				
No		Referent		Referent
Yes		1.72 (1.30-2.27)		1.40 (1.05-1.86)
Polydrug Use				
No		Referent		Referent
Yes		1.27 (0.99-1.63)		1.18 (0.92-1.51)
Childhood Maltreatment				
No		Referent		Referent
Yes		1.54 (1.19-1.99)		1.32 (1.02-1.71)

†Survey commands accounting for stratification, clustering, and unequal selection probabilities yielded nationally representative estimates.



methamphetamine use was an independent predictor of Wave IV depression (AOR: 1.81, 95% CI: 1.12-2.92) (Table 2, Model 4).

*Covariates.* In this model, Wave III depression, being African American, living in functional poverty, and experiencing childhood maltreatment were all associated with increased risk of depression at Wave IV (Table 2, Model 4).

### **Associations Between Methamphetamine Use and Depression, with Gender as a Moderator**

*Model 1.* Adjusted analyses, controlling for gender, revealed that Wave III methamphetamine use was associated with an increased risk of Wave IV depression (AOR: 2.39, 95% CI: 1.55-3.67).

Moderator. The interaction term for gender was not significant.

*Model 2.* Adjusted analyses (covariates included gender, age, race/ethnicity, US region, functional poverty, polydrug use, and childhood maltreatment) revealed that methamphetamine use at Wave III was an independent predictor of subsequent depression at Wave IV (AOR: 2.04, 95% CI: 1.29-3.21) (Table 3, Model 2).

Moderator. The interaction term for gender was not significant.

Covariates. In this model, being African American, living in functional poverty, and experiencing childhood maltreatment were all associated with an increased likelihood of depression at Wave IV (Table 3, Model 2).

*Model 3.* Adjusted analyses, controlling for gender and Wave III depression, revealed that Wave III methamphetamine use was associated with an increased likelihood of Wave IV depression (AOR: 1.90, 95% CI: 1.20-3.00) (Table 3, Model 3).

Moderator. The interaction term for gender was not significant.

*Table 3. Associations Between Methamphetamine Use and Depression Among Young Adults (N=8,688) in the US, with Gender as a Moderator†*

	Model 1	Model 2	Model 3	Model 4
<b>Exposure</b>				
Wave III Meth	2.87 (1.71-4.81)	2.40 (1.38-4.17)	1.88 (1.03-3.43)	1.78 (0.97-3.27)
<b>Hypothesized Moderator</b>				
Gender	0.54 (0.42-0.70)	0.54 (0.42-0.70)	0.61 (0.47-0.79)	0.60 (0.46-0.77)
<b>Interaction Term</b>				
MethXGender	0.70 (0.30-1.65)	0.73 (0.31-1.71)	1.03 (0.42-2.51)	1.04 (0.44-2.46)
<b>Covariates</b>				
Wave III Depression			5.05 (3.95-6.46)	4.69 (3.64-6.04)
Age				
18-20		Referent		Referent
21-22		1.10 (0.85-1.44)		1.08 (0.83-1.41)
23-28		1.12 (0.84-1.49)		1.19 (0.89-1.59)
Race				
White		Referent		Referent
African American		1.80 (1.19-2.72)		1.64 (1.11-2.42)
Latino		0.99 (0.72-1.36)		0.83 (0.59-1.17)
Native American		1.12 (0.36-3.51)		1.15 (0.42-3.12)
Asian		0.82 (0.46-1.44)		0.73 (0.43-1.25)
US Region				
Northeast		Referent		Referent
Midwest		0.98 (0.55-1.74)		1.06 (0.61-1.84)
South		1.00 (0.53-1.89)		1.05 (0.57-1.93)
West		0.94 (0.52-1.68)		0.95-0.53-1.67)
Functional Poverty				
No		Referent		Referent
Yes		1.72 (1.30-2.27)		1.40 (1.05-1.86)
Polydrug Use				
No		Referent		Referent
Yes		1.27 (0.99-1.63)		1.18 (0.92-1.51)
Childhood Maltreatment				
No		Referent		Referent
Yes		1.54 (1.19-1.99)		1.32 (1.02-1.71)

†Survey commands accounted for stratification, clustering, and unequal selection probabilities yielded nationally representative estimates.

Covariates. In this model, Wave III depression was associated with an increased likelihood of Wave IV depression (Table 3, Model 3).

*Model 4.* Adjusted analyses, controlling for covariates and Wave III depression), revealed that methamphetamine use at Wave III was predictive of Wave IV depression (AOR: 1.81, 95% CI: 1.12-2.92) (Table 3, Model 4).

Moderator. The interaction term for gender was not significant.

Covariates. In this model, Wave III depression, being African American, living in functional poverty, and experiencing childhood maltreatment were all variables associated with an increased risk of depression at Wave IV (Table 3, Model 4).

### **Associations Between Methamphetamine Use and Depression, with Functional Poverty as a Moderator**

*Model 1.* Adjusted analyses, controlling for functional poverty, revealed that Wave III methamphetamine use was associated with an increased likelihood of depression at Wave IV (AOR: 2.03, 95% CI: 1.31-3.17) (Table 4, Model 1).

Moderator. The interaction term for functional poverty was not significant (Table 4, Model 1).

Covariates. In this model, functional poverty was associated with an increased risk of depression at Wave IV (Table 4, Model 1).

*Model 2.* Adjusted analyses, controlling for functional poverty, gender, age, race/ethnicity, US region, polydrug use and childhood maltreatment, revealed that methamphetamine use was an independent predictor of Wave IV depression (AOR: 2.04, 95% CI: 1.29-3.21) (Table 4, Model 2).

*Table 4. Associations Between Methamphetamine Use and Depression Among Young Adults (N=8,688) in the US, with Functional Poverty as a Moderator†*

	Model 1	Model 2	Model 3	Model 4
<b>Exposure</b>				
Wave III Meth	2.29 (1.36-3.87)	2.26 (1.31-3.88)	1.87 (1.11-3.15)	1.90 (1.09-3.33)
<b>Hypothesized Moderator</b>				
Functional Poverty	2.18 (1.65-2.89)	1.76 (1.31-2.36)	1.65 (1.23-2.21)	1.41 (1.05-1.90)
<b>Interaction Term</b>				
MethXFunctional Poverty	0.62 (0.20-1.91)	0.66 (0.22-1.96)	0.77 (0.27-2.23)	0.81 (0.29-2.28)
<b>Covariates</b>				
Wave III Depression			5.00 (3.91-6.40)	4.68 (3.64-6.02)
Gender				
Female		Referent		Referent
Male		0.53 (0.41-0.68)		0.60 (0.47-0.77)
Age				
18-20		Referent		Referent
21-22		1.10 (0.85-1.44)		1.08 (0.83-1.41)
23-28		1.11 (0.84-1.48)		1.19 (0.89-1.59)
Race				
White		Referent		Referent
African American		1.79 (1.18-2.72)		1.64 (1.11-2.42)
Latino		0.99 (0.72-1.36)		0.83 (0.59-1.18)
Native American		1.11 (0.36-3.41)		1.14 (0.42-3.09)
Asian		0.81 (0.46-1.44)		0.73 (0.43-1.26)
US Region				
Northeast		Referent		Referent
Midwest		0.98 (0.55-1.73)		1.06 (0.61-1.84)
South		1.00 (0.53-1.90)		1.05 (0.57-1.93)
West		0.94 (0.52-1.68)		0.95 (0.53-1.67)
Polydrug Use				
No		Referent		Referent
Yes		1.27 (0.99-1.63)		1.18 (0.92-1.51)
Childhood Maltreatment				
No		Referent		Referent
Yes		1.54 (1.19-1.99)		1.32 (1.02-1.71)

†Survey commands accounted for stratification, clustering, and unequal selection probabilities yielded nationally representative estimates.

Moderator. The interaction term for functional poverty was not significant.

Covariates. In this model, living in functional poverty, being African American, and experiencing childhood maltreatment were all factors associated with an increased risk of depression at Wave IV (Table 4, Model 2).

*Model 3.* Adjusted analyses, controlling for functional poverty and Wave III depression, revealed that Wave III methamphetamine use was associated with an increased likelihood of Wave IV depression (AOR: 1.76, 95% CI: 1.12-2.76) (Table 4, Model 3).

Moderator. The interaction term for functional poverty was not significant.

Covariates. In this model, both functional poverty and Wave III depression were associated with an increased likelihood of Wave IV depression (Table 4, Model 3).

*Model 4.* Adjusted analyses, controlling for covariates and Wave III depression, revealed that methamphetamine use was an independent predictor of Wave IV depression (AOR: 1.81, 95% CI: 1.12-2.92) (Table 4, Model 4).

Moderator. The interaction term for functional poverty was not significant.

Covariates. In this model, functional poverty, Wave III depression, being African American, and experiencing childhood maltreatment were associated with an increased likelihood of Wave IV depression (Table 4, Model 4).

### **Associations Between Methamphetamine Use and Depression, with Polydrug Use as a Moderator**

*Model 1.* Adjusted analyses, controlling for polydrug use, revealed that Wave III methamphetamine use was associated with an increased likelihood of depression at Wave IV (AOR: 1.90, 95% CI: 1.23-2.94) (Table 5, Model 1).

Table 5. Associations Between Methamphetamine Use and Depression Among Young Adults (N=8,688) in the US, with Polydrug Use as a Moderator†

	Model 1	Model 2	Model 3	Model 4
<b>Exposure</b>				
Wave III Meth	9.40 (1.65-53.56)	13.04 (1.92-88.35)	11.68 (2.02-67.68)	16.08 (2.52-102.61)
<b>Hypothesized Moderator</b>				
Polydrug Use*	1.22 (0.95-1.56)	1.29 (1.01-1.66)	1.12 (0.87-1.43)	1.20 (0.94-1.54)
<b>Interaction Term</b>				
MethXPolydrug Use	0.19 (0.03-1.15)	0.14 (0.02-1.06)	0.13 (0.02-0.84)	0.10 (0.01-0.73)
	<i>Polydrug User:</i> 1.76 (1.13-2.76)	<i>Polydrug User:</i> 1.88 (1.17-3.01)	<i>Polydrug User:</i> 1.54 (0.97-2.45)	<i>Polydrug User:</i> 1.65 (1.00-2.70)
	<i>Non-Polydrug User:</i> 9.40 (1.65-53.56)	<i>Non-Polydrug User:</i> 13.03 (1.92-88.35)	<i>Non-Polydrug User:</i> 11.68 (2.02-67.68)	<i>Non-Polydrug User:</i> 16.08 (2.52-102.61)
<b>Covariates</b>				
Wave III Depression			5.29 (4.16-2.73)	4.71 (3.66-6.06)
Gender				
Female		Referent		Referent
Male		0.53 (0.41-0.67)		0.60 (0.47-0.76)
Age				
18-20		Referent		Referent
21-22		1.10 (0.84-1.43)		1.08 (0.82-1.40)
23-28		1.11 (0.83-1.48)		1.19 (0.89-1.58)
Race				
White		Referent		Referent
African American		1.80 (1.19-2.72)		1.64 (1.11-2.42)
Latino		0.98 (0.71-1.34)		0.82 (0.58-1.16)
Native American		1.05 (0.33-3.29)		1.06 (0.38-2.93)
Asian		0.80 (1.19-2.72)		0.72 (0.42-1.25)
US Region				
Northeast		Referent		Referent
Midwest		0.98 (0.55-1.74)		1.06 (0.61-1.85)
South		1.01 (0.53-1.90)		1.05 (0.57-1.94)
West		0.94 (0.52-1.70)		0.95 (0.53-1.68)
Functional poverty				
No		Referent		Referent
Yes		1.72 (1.31-2.27)		1.40 (1.05-1.86)
Childhood maltreatment				
No		Referent		Referent
Yes		1.54 (1.19-1.99)		1.32 (1.02-1.70)

†Survey commands accounted for stratification, clustering, and unequal selection probabilities yielded nationally representative estimates.

\*Polydrug use interaction significant at the p<0.05 level.

Moderator. The interaction term for polydrug use was significant at the 0.05 level. Methamphetamine users who *were not* polydrug users had higher increased odds of depression (AOR: 9.04, 95% CI 1.65-53.56) than polydrug using methamphetamine users (AOR: 1.76, 95% CI: 1.13-2.76). While methamphetamine only users appeared to be at a considerably higher risk of depression, being nine times more likely than poly-drug using methamphetamine users to become depressed, it is important to note the large confidence interval for this odds ratio, which may be a function of the small number of non-poly drug using meth users (n=8) (Table 5, Model 1).

*Model 2.* Adjusted analyses, controlling for all covariates, revealed that Wave III methamphetamine users are two times more likely to experience depression at Wave IV compared to non-methamphetamine users (AOR: 2.04, 95% CI: 1.29-3.21) (Table 5, Model 2).

Moderator. The interaction term for polydrug use was significant at the 0.05 level. Methamphetamine users who were not polydrug users had thirteen times the odds of depression at Wave III (AOR: 13.03, 95% CI: 1.92-88.35). Methamphetamine users that were also polydrug users had increased odds of depression, though not as high as the non-polydrug users (AOR: 1.88, 95% CI: 1.17-3.01) As mentioned above, it is important to note the wide confidence interval for non-polydrug methamphetamine users, noting that although they are thirteen times more likely to become depressed, this odds ratio may be a function of the small number of non-polydrug users (n=8) (Table 5, Model 2).

Covariates. Being African American, living in functional poverty, and experiencing childhood maltreatment were all associated with Wave IV depression (Table 5, Model 2).

*Model 3.* Adjusted analyses, controlling for all polydrug use and Wave III depression, revealed that Wave III methamphetamine users have increased odds of depression at Wave IV compared to non-methamphetamine users (AOR: 1.68, 95% CI: 1.07-2.64) (Table 5, Model 3).

Moderator. The interaction term for polydrug use was significant at the 0.05 level. Methamphetamine users who *were not* polydrug users had nearly twelve times the odds of depression at Wave III (AOR: 11.68, 95% CI: 2.02-67.68). The odds ratio for polydrug users was not significant (AOR: 1.54, 95% CI: 0.97-2.45). Again, it should be noted that non-polydrug methamphetamine users had nearly twelve times the odds of becoming depressed, however the precision of the estimate may not be accurate as the confidence interval was wide and there were only 8 non-polydrug methamphetamine users (Table 5, Model 3).

Covariates. In this model, Wave III depression was associated with an increased risk of depression at Wave IV (Table 5, Model 3).

*Model 4.* Adjusted analyses, controlling for all covariates and Wave III depression, revealed that methamphetamine users were nearly two times more likely to be depressed at Wave IV compared to those who did not use methamphetamine (AOR: 1.81, 95% CI: 1.12-2.92) (Table 5, Model 4).

Moderator. The interaction term for polydrug use was significant at the 0.05 level. Methamphetamine users who *were not* polydrug users had sixteen times the odds of depression at Wave III (AOR: 16.08, 95% CI: 2.52-102.61). Non-polydrug methamphetamine users were less than two times as likely to be depressed at Wave IV (AOR: 1.65, 95% CI: 1.00-2.70). It is important to note the large confidence interval for



this odds ratio, which may be a function of the small number of non-poly drug using meth users (n=8) (Table 5, Model 4).

Covariates. In this model, Wave III depression, being African American, living in functional poverty, and experiencing childhood maltreatment were all factors associated with Wave IV depression (Table 5, Model 4).

## **Associations Between Methamphetamine Use and Depression, with Childhood**

### **Maltreatment as a Moderator**

*Model 1.* Adjusted analyses, controlling for childhood maltreatment, revealed that methamphetamine use at Wave III was associated with an increased likelihood of depression at Wave IV (AOR: 1.91, 95% CI: 1.23-2.98) (Table 6, Model 1).

Moderator. The interaction term for childhood maltreatment was not significant.

Covariates. In this model, experiencing childhood maltreatment was associated with an increased risk of depression at Wave IV (Table 6, Model 1).

*Model 2.* Adjusted analyses (controlling for childhood maltreatment, gender, age, race/ethnicity, US region, functional poverty, and polydrug use) revealed that methamphetamine use at Wave III was associated with an increased risk of Wave IV depression (AOR: 2.04, 95% CI: 1.29-3.21) (Table 6, Model 2).

Moderator. The interaction term for childhood maltreatment was not significant.

Covariates. In this model, experiencing childhood maltreatment, being African American, and living in functional poverty were associated with an increased likelihood of depression at Wave IV (Table 6, Model 2).

*Table 6. Associations Between Methamphetamine Use and Depression Among Young Adults (N=8,688) in the US, with Childhood Maltreatment as a Moderator†*

	Model 1	Model 2	Model 3	Model 4
<b>Exposure</b>				
Wave III Meth	2.38 (1.37-4.14)	2.49 (1.42-4.39)	2.05 (1.12-3.75)	2.24 (1.19-4.20)
<b>Hypothesized Moderator</b>				
Childhood Maltreatment	1.72 (1.34-2.20)	1.60 (1.23-2.07)	1.40 (1.09-1.79)	1.37 (1.06-1.77)
<b>Interaction Term</b>				
MethXChildhood Maltreatment	0.58 (0.22-1.50)	0.60 (0.23-1.56)	0.60 (0.23-1.53)	0.59 (0.23-1.51)
<b>Covariates</b>				
Wave III Depression			5.14 (4.03-6.55)	4.69 (3.65-6.03)
Gender				
Female		Referent		Referent
Male		0.53 (0.41-0.68)		0.60 (0.47-0.77)
Age				
18-20		Referent		Referent
21-22		1.10 (0.84-1.43)		1.08 (0.83-1.41)
23-28		1.11 (0.83-1.48)		1.19 (0.89-1.58)
Race				
White		Referent		Referent
African American		1.79 (1.19-2.71)		1.63 (1.10-2.42)
Latino		0.99 (0.72-1.35)		0.83 (0.59-1.18)
Native American		1.15 (0.37-3.59)		1.16 (0.43-1.26)
Asian		0.81 (0.46-1.43)		0.73 (0.43-1.26)
US Region				
Northeast		Referent		Referent
Midwest		0.97 (0.55-1.73)		1.05 (0.60-1.83)
South		1.00 (0.53-1.89)		1.04 (0.57-1.92)
West		0.92 (0.52-1.66)		0.93 (0.53-1.64)
Functional poverty				
No		Referent		Referent
Yes		1.72 (1.30-2.26)		1.39 (1.05-1.85)
Polydrug use				
No		Referent		Referent
Yes		1.27 (0.99-1.63)		1.18 (0.92-1.51)

†Survey commands accounted for stratification, clustering, and unequal selection probabilities yielded nationally representative estimates.

Moderator. The interaction term for childhood maltreatment was not significant.

Covariates. In this model, experiencing childhood maltreatment and being depressed at Wave III were both factors associated with an increased likelihood of Wave IV depression (Table 6, Model 3).

*Model 4.* Adjusted analyses, controlling for covariates and Wave III depression, revealed that methamphetamine use at Wave III is an independent predictor of depression at Wave IV (AOR: 1.81, 95% CI: 1.12-2.92) (Table 6, Model 4).

Moderator. The interaction term for childhood maltreatment was not significant.

Covariates. In this model, experiencing childhood maltreatment, being depressed at Wave III, being African American, and living in functional poverty were all associated with an increased risk of depression at Wave IV (Table 6, Model 4).

## CHAPTER 5: DISCUSSION

### Summary of Findings and Implications

This study used a nationally representative dataset of young adults, the age group most likely to use methamphetamine (SAMHSA, 2006), to examine the longitudinal relationship between past year methamphetamine use and depression. Although previous research has identified an association between methamphetamine use and depression, these studies typically involved clinical populations in treatment or criminal justice populations (Glasner-Edwards et al., 2008; Semple, Patterson & Grant, 2005; Zweben et al., 2004). To the author's knowledge, no research exists examining the association between methamphetamine use and depression within the general population.

Further, little is known about additional factors that may affect the relationship, variables that either increase the risk of depression or act as a buffer, potentially diminishing the risk of depression for methamphetamine users. In this study analyses were conducted to determine whether the association between methamphetamine use and depression exists within the general population and to examine how other factors may affect this relationship. The specific factors examined included gender, functional poverty status, polydrug use, and childhood maltreatment.

Indeed, this study provides evidence that among methamphetamine users in the general population, methamphetamine use is associated with an increased risk of depression. Further, longitudinal analyses revealed that methamphetamine use is an independent predictor of future depression, when controlling for covariates including gender, age, race/ethnicity, US region, functional poverty, childhood maltreatment, and polydrug use. Lastly, analyses controlling for depression at Wave III revealed that

independent of depression status, methamphetamine users are more likely to be depressed at Wave IV (six years later).

Additionally, aside from polydrug use, none of the other potential moderator variables were significant, and therefore, gender, functional poverty, and childhood maltreatment do not contribute to nor buffer against depression for methamphetamine users. Given these findings, designing interventions and treatment programs for depression that are targeted at specific populations of methamphetamine users may not be as important as incorporating mental health treatment for all methamphetamine users.

In fact, given the increased risk for depression among methamphetamine users, individuals in treatment programs may benefit from focusing on mental health outcomes as part of substance abuse treatment interventions. At the very least, this study highlights the need for appropriate screening and diagnoses of depression among methamphetamine users and future studies focusing on outcomes for depressed methamphetamine users will provide a more complete picture of the problem.

Polydrug use was found to be a moderator of depression, as exclusive methamphetamine users (those who were *not* polydrug users) were more likely to be depressed at Wave IV compared to polydrug users. However, the number of non-polydrug methamphetamine users was very small (n=8), which resulted in a large confidence interval and imprecise measurement. Therefore this finding is suspect and warrants further investigation.

The findings have several implications for future research. First, this study used Waves III (2001-02) and IV (2007-08) of Add Health, as it was the most comprehensive dataset available to answer the research questions. However, the six year time lapse

between waves allows for many other life events and changes, such as death of a loved one, divorce, or job loss. These factors may result in residual confounding. Future research should involve a time series design with more frequent measurement over the longitudinal period.

Since this study controlled for many socio-behavioral factors associated with depression, these findings add further support to theories highlighting the role of the brain and neurocognitive functioning in depression among methamphetamine users. There is a body of research focused on the effects of methamphetamine abuse and dependence on the brain (see Meredith, et al., 2005); however, many of the published studies focus on clinical samples or criminal justice populations. Designing studies to look at methamphetamine users in the general population is warranted, given the findings of this study.

The ecological model was used as a framework to guide the selection of different level variables to test as potential moderators. Although none of the variables tested were shown to moderate the association between methamphetamine use and depression, further research evaluating additional variables is warranted. The Add Health dataset is rich with information on microsystem level factors (e.g. criminal justice involvement), mesosystem level factors (e.g. relationship history), and exosystem level factors (e.g. neighborhood characteristics). In the Add Health data, information on macrosystem level variables is limited, however, it may be that the former mentioned levels are more appropriate for identifying information that can be used to develop prevention or treatment programs. Lastly, using the ecological model, several variables were tested as potential moderators of the relationship between methamphetamine use and depression;

however, it may be that another relationship, such as mediation, exists in these data.

Additional research and analyses are needed to fully understand the association and how other factors may affect it.

As previously stated, methamphetamine use is associated with significant physical and mental health consequences. Aneshensel and colleagues (1984) assessed physical health and depression among a community sample of 744 adults. Findings indicated that physical health problems were associated with increased levels of depression, even after controlling for previous depression (Aneshensel, Frerisch & Huba, 1984). The association between depression and physical illness has been described as a self-perpetuating and mutually reinforcing process operating over time (Aneshensel, Frerisch & Huba, 1984). In terms of methamphetamine use, it is possible that the negative health consequences and physical ailments associated with use (e.g. hypertension, insomnia) lead to depression. This may be a potential area of future research.

### **Limitations**

This study is not without limitations that must be noted. First, although the findings from this study are generalizable as the sample was nationally representative, it is likely that those with the most severe drug problems or mental health issues were not found for follow-up interview and the final sample may not accurately capture those with the most severe symptoms. Second, this study employed a broad measurement for methamphetamine use (any use in the past year) to generate a larger sample size. The methamphetamine use variable is simply “any use” and does not account for frequency or duration of use, nor does it allow for assumptions about abuse or dependence. Further research accounting for these factors will allow for better application of the findings.

Third, this study is based on self-report data, which may result in underreporting of socially undesirable behaviors, such as substance use and depressive symptoms. However, Add Health methodology includes precautions to increase confidentiality through the use of audio computer-assisted self-interview (A-CASI), which is associated with increased reporting of sensitive information (Turner, Ku, Lindberg, Pleck, & Sonenstein, 1998).

### **Conclusions**

Despite the noted limitations, this study addresses a critical gap in the literature, as the findings establish that methamphetamine use increases the risk for later depression and even independently predicts future depression. In addition, this study revealed that certain factors, including gender, functional poverty, and childhood maltreatment, have no effect on the association between methamphetamine use and depression. Establishing the association between methamphetamine use and depression in a nationally representative sample, and identifying that the risk of depression is not moderated by several socio-behavioral factors, are necessary preliminary steps for developing and delivering interventions for both prevention and treatment purposes.



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