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Self-efficacy Mediates the Relationship of Neurocognitive Impairment and HIV Risk Reduction Intervention Outcomes among Female High-risk Drug Users in Treatment

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DEDICATION

I would like to dedicate my thesis to my mother "Feruja Begum" who made unlimited sacrifices to raise me and my brother.

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Finally, my acknowledgement goes to my funding source, National Institute on Drug Abuse (NIDA).

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ABBREVIATIONS

Abbreviations:

ACASI	Audio Computer Assisted Self-Interview
ACME	Average Causal Mediation Effect
ADE	Average Direct Effect
AIDS	Acquired Immunodeficiency Syndrome
ANI	Asymptomatic Neurocognitive Impairment
ART	Anti-Retroviral Therapy
BINI	Brief Inventory of Neurocognitive Impairment
CART	Combination Anti-retroviral Therapy
CDC	Center for Disease Control and Prevention
CHRP	Community Friendly Health Recovery Program
CNU	Clean Needle Use
CU	Condom Use
DV	Dependent Variable
EBI	Evidence Based Intervention
FSWs-IDUs	Female Sex Workers Who Inject Drugs
HAART	Highly Active Anti-Retroviral Therapy
HAD	HIV Associated Dementia
HAND	HIV Associated Neurocognitive Impairment
HIV	Human Immunodeficiency Virus
IDU	Injection Drug Use
IRB	Institutional Review Board
IMB	Information-Motivation-Behavioral Skills
IV	Independent Variable
Me	Mediator
MMT	Methadone Maintenance Therapy

MND	Mild Neurocognitive Disorder
Mo	Moderator
MSM	Men Who Have Sex with Man
NCI	Neurocognitive Impairment.
NIDA	National Institute on Drug Abuse
NIH	National Institute of Health
NIS	Neuropsychological Impairment Scale
OUDs	Opioid Use Disorders
PLWH	People Living With HIV
PrEP	Pre-Exposure Prophylaxis
PWID	People Who Inject Drug
SAMHSA	Substance Abuse and Mental Health Services Administration
SISE	Safe Injection Self-Efficacy
SSSE	Safe Sex Self-Efficacy
TE	Total Effect
UNAIDS	United Nations Program on HIV and AIDS
WHO	World Health Organization

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ABSTRACT

Background: Prior research has widely recognized neurocognitive impairment (NCI), HIV risk reduction self-efficacy, and gender as important predictors of HIV risk reduction intervention outcomes. No studies to date, however, have explored how these variables interact with each other, and the combined effects when taken together on HIV risk reduction behaviors. This paper incorporated a moderated mediation model to examine whether the indirect effect of NCI on HIV risk reduction intervention outcomes via self-efficacy related to HIV risk reduction varies by gender among people who use drugs (PWUDs) in treatment.

Method: Two hundred and thirty six HIV-negative opioid-dependent individuals newly enrolled in a methadone maintenance treatment (MMT) and reporting drug- and/or sex-related HIV risk behaviors completed an audio-computer-assisted self-interview (ACASI) that measured NCI, HIV risk reduction self-efficacy (i.e., drug and sex-related) and HIV risk reduction outcomes (i.e., drug- and sex-related) over time. We used a linear model path analytic framework to test the moderated mediation models for drug- and sex-related HIV risk reduction variables (i.e., clean needle use and consistent condom use).

Results: Results showed that a higher degree of NCI significantly predicted lower levels of safe injection self-efficacy (β=-0.0160, p=0.0160) and clean needle use (β=-0.006, p=0.03). Moreover, the indirect effect of NCI on clean needle use was mediated via safe injection self-efficacy (β=-0.0016, p=0.02, proportion mediated = 25%). Similarly, a higher degree of NCI significantly predicted lower levels of safe sex self-efficacy (β=-0.0231, p=0.0238), but not condom use (β=-0.0008, p=0.81). However, the indirect effect of NCI on consistent condom

use was mediated via safe sex self-efficacy (β=-0.003, p=0.02, proportion mediated = 59%). Further, these effects were moderated by gender, with only females showing significant mediation effects of self-efficacy for both clean needle use and condom use.

Conclusion: The findings make an important contribution to our understanding of the utility of a moderated mediation model. Our model showed, such that there was a differential indirect effect of NCI on HIV risk reduction intervention outcomes via self-efficacy between males and females.

CHAPTER 1 : Introduction

Despite a wide array of preventive efforts, approximately 50,000 new HIV infections are diagnosed per year in the United States. (Centers for Disease Control and Prevention, 2014). From the beginning of HIV era, drug abuse has been a well-established risk factor of HIV infection (Centers for Disease Control and Prevention, 2013). People who use drugs (PWUDs) represent a critical conduit for the transmission of new HIV infection through drug-related (e.g., needle sharing) and sex-related (e.g., inconsistent condom use) HIV risk behaviors (Arasteh, Des Jarlais, & Perlis, 2008; Baron & Kenny, 1986; Li et al., 2013; Marshall et al., 2014; Mateu-Gelabert et al., 2016; Noar, 2008; Pitpitan et al., 2015; Strathdee et al., 2010; Volkow & Montaner, 2011). Although the number of new HIV infections attributed to PWUDs has decreased in recent years (Centers for Disease Control and Prevention, 2014), they still remain as priority populations for prevention of HIV because of their significant association with HIV risk behaviors.

Prior research suggests both drug abuse and HIV infection can lead to neurocognitive impairment (NCI) (Anand, Springer, Copenhaver, & Altice, 2010; Antinori et al., 2007; Clifford & Ances, 2013; Heaton et al., 2011; Indlekofer et al., 2009; Lundqvist, 2005; Schouten, Cinque, Gisslen, Reiss, & Portegies, 2011; Vik, Cellucci, Jarchow, & Hedt, 2004; Woicik et

al., 2009) that exhibited a noteworthy association with drug-related and sex-related HIV risk behaviors (Anand et al., 2010; Mitchell, Severtson, & Latimer, 2007; Shrestha & Copenhaver, 2016; Stacy, Newcomb, & Ames, 2000). In addition, NCI reduces medication adherence (Anand et al., 2010; Ezeabogu, Copenhaver, & Potrepka, 2012; Lovejoy & Suhr, 2009). Overall, increased risk behaviors and suboptimal adherence demonstrated by individuals who have NCI diminishes the effectiveness of interventions aimed to reduce new HIV infection (Anand et al., 2010; Shrestha, Huedo-Medina, & Copenhaver, 2015). Furthermore, HIV prevention interventions often involve learning and retaining new information, inhibiting impulsive responses, and engaging in future-oriented behaviors that place high demand on various cognitive domains, like memory, learning, and attention. Among drug users, however, neurocognitive domains that are commonly compromised include executive functioning, information processing, motor functioning, attention, learning, and memory (Anand et al., 2010; Lovejoy & Suhr, 2009). Impairment of these domains also can negatively influence the potency of the intervention. Given the impact of NCI on intervention effectiveness, it is crucial to understand the underlying mechanisms through which NCI may influence treatment outcomes.

One construct thought to be important in promoting positive intervention outcomes is self-efficacy - developing a sense of personal power to exercise control over situations, including risk reduction skills (Bandura, 1990). Prior research has shown self-efficacy to be a strong predictor of improved treatment outcomes (Bandura, 1990; Burleson & Kaminer, 2005), and lower self-efficacy is associated with higher levels of HIV risk behaviors (Bedoya et al., 2012; Nehl, Klein, Sterk, & Elifson, 2015; Puffer et al., 2011; Thomas et al., 2009; Winningham et al., 2004). Self-efficacy has been shown to serve as a mediator between norms for condom

use and unsafe sex (Miner, Peterson, Welles, Jacoby, & Rosser, 2009), and intervention significantly influenced needle sharing via safe injection self-efficacy (Pitpitan et al., 2015). Thus, it is important to examine the extent to which self-efficacy stemming from behavioral interventions may be negatively influenced by a participant's NCI, as is expected based on recent work in this area (Worley, Tata, Granholm, & Brown, 2014). To date, very few studies have examined how NCI may influence self-efficacy and, ultimately, treatment outcomes.

Another construct of relevance to intervention outcomes pertains to gender. Gender difference plays a significant role in both self-efficacy and intervention outcomes (Buchanan et al., 2006; M. M. Copenhaver, Lee, & Baldwin, 2013; Corsi et al., 2014; Lee, Salman, & Cooksey-James, 2016; Puffer et al., 2011; Stevens, Murphy, & McKnight, 2003; Zandmomen et al., 2014). Moreover, some studies report greater NCI in women than men (Gandhi et al., 2010; Royal et al., 2016; Shrestha et al., 2015; Troncoso & Conterno, 2015). Thus, examining the interacting effects of gender, NCI, and self-efficacy on HIV risk behavior is of particular relevance to future intervention efforts.

The purpose of the present study is to explore the indirect effect of NCI on HIV preventive behaviors (i.e., clean needle use and condom use) via self-efficacy. Given the established relationship between gender with NCI, self-efficacy, and HIV risk behavior (Buchanan et al., 2006; M. M. Copenhaver et al., 2013; Corsi et al., 2014; Gandhi et al., 2010; Lee et al., 2016; Puffer et al., 2011; Royal et al., 2016; Shrestha et al., 2015; Stevens et al., 2003; Troncoso & Conterno, 2015; Zandmomen et al., 2014), we also aim to explore whether this indirect effect is moderated by gender.

CHAPTER 2 : Literature Review

2.1 HIV Prevalence

Molecular epidemiologic studies attempted to give an insight into the origin and geographic diffusion patterns of HIV infection (Inrig, 2015). The virus is assumed to have entered human populations through cross-species transmission of related chimpanzee retroviruses found in western equatorial Africa in the early twentieth century (Sharp & Hahn, 2011). From the beginning of HIV epidemic, Sub-Saharan Africa is the most severely affected region, accounting for 71% of all new HIV infections in 2008 (Unaids, 2009).

As a whole, the HIV epidemic has changed over the past 20 years, from the highest estimated new infections of 3.7 million in 1997, to declining new infections and AIDS-related mortality throughout the 2000s (Figure 1) (Unaids, 2013). There were 2.1 million new HIV infections in 2013 - a decline of 38% from 2001, when there were around 3.4 million new infections (UNAIDS, 2014). Among 35 million people living with HIV infection globally in 2013, 46% were women or girls elder than 15 years. At the end of 2013, 12.9 million people

receiving antiretroviral therapy globally. As more people are receiving life-saving antiretroviral therapy, there was a decline in the number of AIDS deaths with 1.5 million in 2013 from 2.3 million in 2005, when the highest number of deaths were recorded. As a result, there was an increase in people living with HIV from previous years (Figure 2). Advancement has been dramatic in decreasing new HIV infections among children. In 2013, about 240 000 children were newly infected with HIV, which is 58% lower than in 2002, when the highest number of children, around 580 000, became newly infected with HIV (UNAIDS, 2014). Though HIV incidence is declining, certain group of populations are at high risk of being infected. World Health Organization (WHO) defined five key populations who are at increased risk of HIV. Usually, the social and legal issues related to their behaviors increase their susceptibility to HIV, irrespective of the epidemic type or local context. The five key populations include men who have sex with men (MSM), people who inject drugs (PWIDs), people in prisons and other closed settings, sex workers, and transgender people (WHO, 2014). Recent studies indicated elevated level of infections in these populations nearly in all regions (Unaids, 2009).

In the United States, more than 1.2 million people are living with HIV and 12.8% of them are unware of their status. The estimated new HIV infection has remained stable in recent years – at about 50,000 per year. But the rate of new infection is particularly high among certain groups. Gay, bisexual, and other men who have sex with men (MSM) bears the greatest burden of HIV infection and African Americans are disproportionately affected. MSM represented 78% of new HIV infections among males and 63% of all new infections in 2010. On the other hand, among females, major route of transmission of HIV were heterosexual contact (84%) or injection drug use (16%) in 2010. Overall, injection drug users accounted for 8% of new HIV infections in 2010 and 15% of those living with HIV in 2011 (CDC, 2015). HIV incidence is

concentrated primarily in large U.S. metropolitan areas (81% in 2011), with New York, Los Angeles, and Miami topping the list. Regionally, the incidence is highest in the South, accounted for about half (48%) of new HIV diagnoses in 2011. But taking population into account, the rate is highest in the Northeast followed by South, West and Mid-west (Centers for Disease Control and Prevention, 2014).

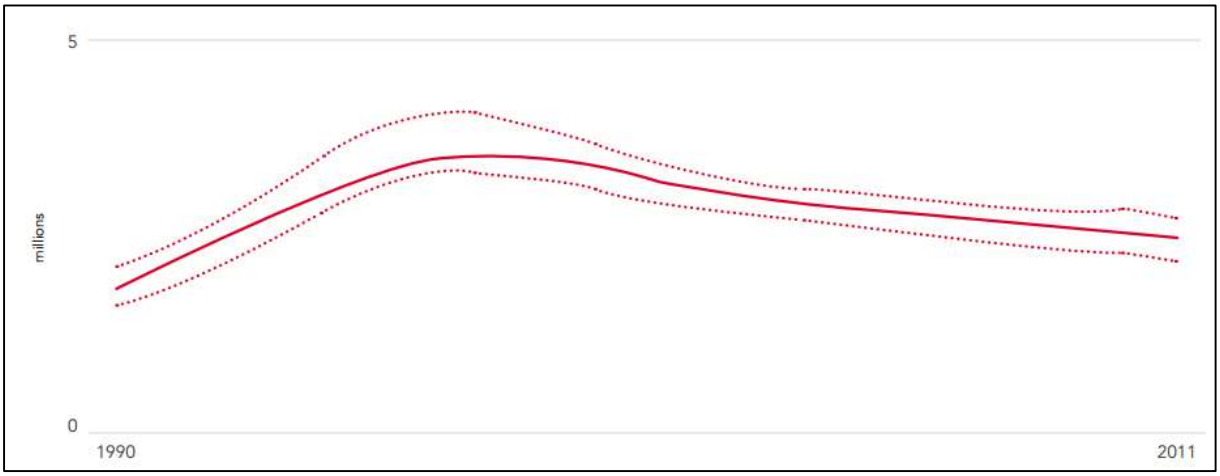

Figure 1: Number of people newly infected with HIV [Global, 1990-2011]

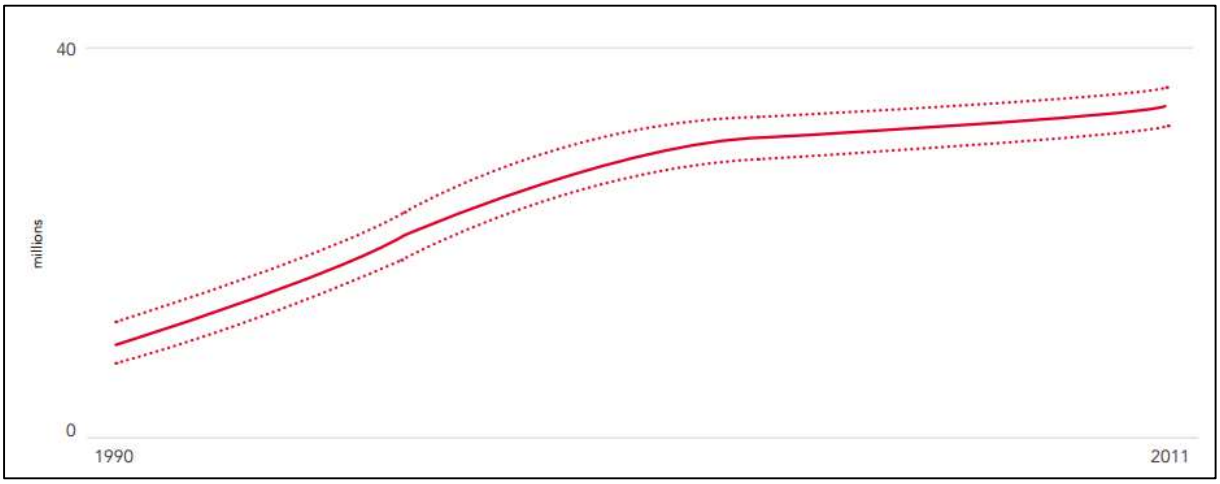

Figure 2: Number of people living with HIV [Global, 1990-2011]

2.2 HIV and Substance Abuse

Substance abuse, is defined as the use of illicit and self-damaging recreational or prescription drugs or chemicals that lead to an inability to control the use of that substance. From the beginning of HIV epidemic, substance use, abuse, and dependence have been a well-established risk factor of HIV infection. Injection drug use (IDU) is a direct route of transmission of HIV (Centers for Disease Control and Prevention, 2013). IDU is responsible for significant proportion of new HIV infections in many parts of the world, including countries in Eastern Europe, South America, and East and Southeast Asia (UNAIDS, 2012). In 2010, 8% of new HIV infections in the United States happened via IDU (Figure 3) and men accounted for 62% of all IDU-associated HIV infections. Half (50%) of the estimated new HIV infection among injection drug users attributed to African Americans, 26% to white, and 21% to Hispanics/Latinos.

HIV can be transmitted in this high risk population by sharing needles, syringes, or other injection equipment (e.g., cookers, rinse water, cotton) that were used by a person living with HIV. Injection drug use also can alter judgement and reduce inhibitions to take part in risky behaviors, like not using condoms or taking preventive medicine, such as pre-exposure prophylaxis (PrEP). In the cities with high HIV prevalence, about one-third of PWID reported sharing syringes, more than half reported sharing other injection equipment, and 72% of female injection drug users reported having sex without a condom in the past 12 months. PWID may also engage in risky sexual behaviors in exchange of drugs (CDC, 2015). Other form of substance abuse, like drinking, smoking, ingesting, or inhaling drugs such as alcohol, crack cocaine, methamphetamine (“meth”), and amyl nitrite (“poppers”) may not directly transmitting HIV, but associated with an increased risk of HIV transmission by reducing users’

self-consciousness to engage in risky sexual behavior (Centers for Disease Control and Prevention, 2013). Studies conducted on IDUs also reported significant association between drug abuse and HIV transmission via injection equipment sharing and unprotected sex. A study conducted by Arasteh et al., evaluated data from 6341 IDUs entering methadone maintenance treatment in New York City between 1990 and 2004. They analyzed the relationship of risky sexual behavior with alcohol intoxication during sex and at-risk drinking (more than 14 drinks per week for males or 7 drinks per week for females) in the past 6 months. They reported more unprotected sex with casual sex partners in both conditions, alcohol intoxication during sex and at-risk drinking in the past 6 months. In case of primary partners, IDUs also reported unprotected sex when both partners were intoxicated (Arasteh et al., 2008). Another cross-sectional study conducted by Mateu-Gelabert et al., assessed injection risk behaviors among heroin injectors in the Colombian cities of Medellín and Pereira. Researchers conducted a structured interview of 60 minutes with local PWID by using WHO-II survey, which has been widely used to study this population and the survey included questions on demographics, drug use and injection equipment sharing behaviors in the previous 6 months, last injection event, and HIV knowledge (WHO, 2000). They have found injection equipment sharing was a common phenomenon among PWID. Forty-eight percent reported syringe sharing and 49% also reported sharing of cookers, filters, or rinse water. Among those who injected with previously used syringe, 31% of them reported never cleaning used syringes and those who cleaned used syringes, only 25% of them used alcohol or cleaning agent. The results of this study indicated a high prevalence of risky drug injecting behavior among injection drug users, such as sharing of injection equipment and not cleaning used syringes before injecting (Mateu-Gelabert et al., 2016). In addition to increasing the risk of HIV transmission via drug- and sex-

related HIV risk behaviors, substance abuse can make individuals more vulnerable to HIV infection. In those who already infected, substance abuse can accelerate disease progression to more advanced clinical stages of HIV infection, marked by a high occurrence of opportunistic infections, non-AIDS-defining illnesses and HIV-related deaths by negatively impacting adherence to treatment (Centers for Disease Control and Prevention, 2013). A systematic review and meta-analysis examined mortality rates and causes of death in PWID, and identified drug overdose and AIDS-related illness to be associated with higher risk of death in this population (Mathers et al., 2013).

Overall, substance abuse is associated with non-adherence, immunosuppression, increased risk behaviors, and increased burdens on health care systems. Approximately 50% of people living with HIV/AIDS reported current or past histories of substance abuse (Figure 4) (NSDUH, 2010). HIV prevalence among injection drug users is highest in Russia (37%), followed by USA (16%) and China (12%) (Mathers et al., 2008). Even though the number of new HIV infections attributed to IDU has reduced in recent years (Centers for Disease Control and Prevention, 2014), this population remains priority for HIV prevention because of their significant association with HIV risk behaviors.

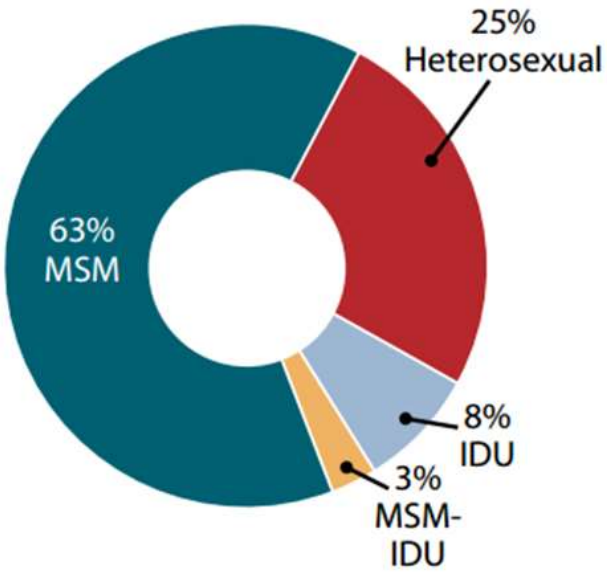

Figure 3: Estimated new HIV infection by transmission category [CDC, 2012]

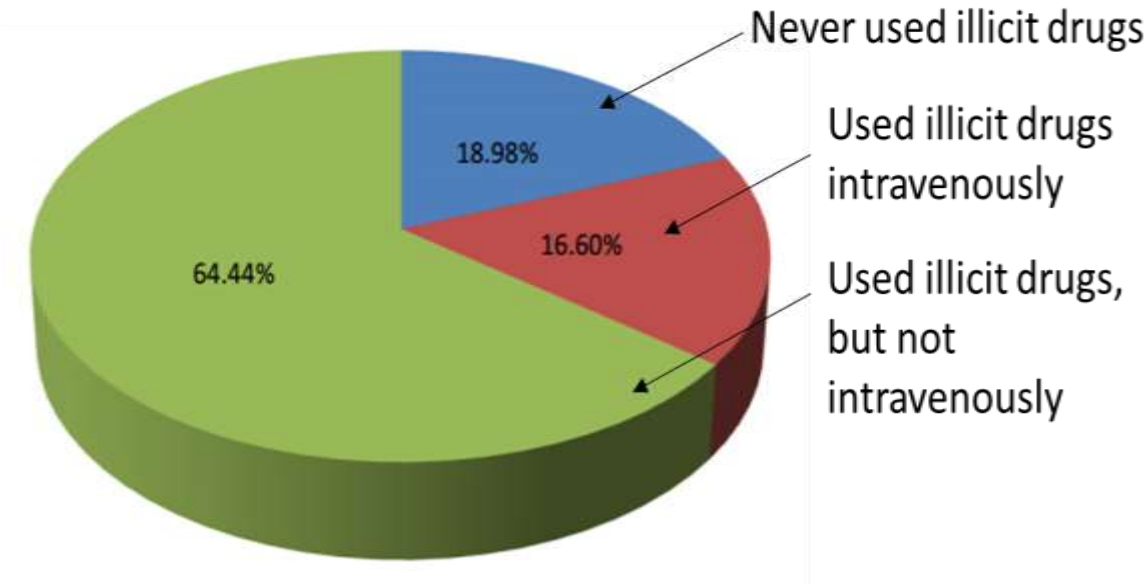

Figure 4: Lifetime drug use in people living with HIV in USA [NSDUH, 2010]

2.3 Substance Abuse, NCI, and HIV

Cognitive impairment is defined as trouble remembering, learning new things, concentrating, or making decisions that affect a persons' everyday life. Cognitive impairment

ranges from mild to severe. With mild impairment, cognitive functions are impaired, but still people are able to do their everyday activities. Severe level of impairment can lead to losing the ability to comprehend the sense or significance of something and the ability to talk or write, eventually resulting in the incapacity to live independently (CDC, 2010). Currently, in United States, more than 16 million people are living with cognitive impairment which places significantly greater demands on health care systems (CDC, 2010). Cognitive impairment is commonly manifested by memory loss, frequently asking the same question or repeating the same story over and over, not recognizing familiar people and places, having trouble exercising judgment, such as knowing what to do in an emergency, changes in mood or behavior, vision problems, and difficulty planning and carrying out tasks (CDC, 2010).

Drug abuse impacts neurocognitive functioning both directly and indirectly. Drugs directly impact neurochemical activity of the brain, alter the level of neurotransmitters, and indirectly impact brain functioning via reducing the cerebral blood flow affecting other organ systems, especially liver and cerebral vasculature. These direct and indirect effects of drugs on the brain can cause different degrees of neurocognitive impairment among drug abusers (Vik et al., 2004). Neurocognitive domains that are commonly compromised by drug abuse include executive functioning, information processing, motor functioning, attention, learning, and memory (Anand et al., 2010). Previous studies exhibited significant performance deficits of attention, executive function, and verbal/working memory in chronic cocaine users (Shrestha et al., 2015; Vonmoos et al., 2013; Woicik et al., 2009). A study aimed to assess the relationship between drug abuse and cognitive functioning showed significant association of ecstasy and cannabis use with poorer episodic memory function and lapses of attention in a dose-related manner (Indlekofer et al., 2009). Another review article also reported loss of attention and

memory in cannabis users and decreased mental flexibility, increased perseveration, and reduced learning, to shift and/or sustain attention to be associated with heavy cannabis use. Amphetamine/methamphetamine use also demonstrated deficits in learning, delayed recall, processing speed, and working memory. MDMA (3,4-methylenedioxymethamphetamine, ecstasy) users showed difficulties in coding information into long-term memory, impaired verbal learning, easy distraction, and loss of attention/focus on complex tasks. The degree and duration of executive impairment increased with the severity of use. Chronic cocaine use caused impairment of attention, learning, memory, reaction time and cognitive flexibility. Heroin addiction might negatively impact impulse control, and selective processing (Lundqvist, 2005).

Drug abuse with HIV infection, especially opioids and cocaine, may deteriorate cognitive functioning by reducing immune system integrity and stimulating viral replication. Cocaine also increases the permeability of the blood–brain barrier to HIV and promotes cellular apoptosis, leading to more neurological impairment (Anand et al., 2010). HIV-associated neurocognitive disorders (HAND) include varying degree of neurocognitive dysfunction, ranging from severe HIV-associated dementia (HAD) to mild neurocognitive disorder (MND) and asymptomatic neurocognitive impairment (ANI). The pattern of HAND has rapidly evolved with the widespread use of antiviral treatment. Before combination antiretroviral therapy (CART), HAD was more common which is defined by increased loss of attention and concentration, marked motor slowing, and multiple behavioral components mostly leading to death in less than a year. During the era of CART, MND and ANI are more common manifestations of HAND. Cognitive impairment related to HAND in CART era is more similar to other common degenerative disorders (i.e. Alzheimer's disease) than HAD. HAND

manifestation from CART era comprised more memory (learning) and executive function impairment (Clifford & Ances, 2013; Heaton et al., 2011).

Approximately half of all treated HIV patients have neurocognitive disorders. Prior studies assessing the neurophysiological status of HIV infected individuals among different risk groups in both European cohort (Chiesi et al., 1996) and American cohort (Nath, Maragos, Avison, Schmitt, & Berger, 2001; Tyor & Middaugh, 1999), reported higher prevalence of cognitive disorder in HIV infected drug users than in other groups. Though, the introduction of CART in 1996 has reduced HIV related severe neurocognitive disorders, such as dementia (Dore, McDonald, Li, Kaldor, & Brew, 2003; Robertson et al., 2007; N. C. Sacktor et al., 1999, 2000), subtle forms of cognitive impairment continues to be a challenge in CART era (Heaton et al., 2011; Robertson et al., 2007; N. Sacktor et al., 2002).

2.4 NCI and HIV Risk Behavior

The pattern of cognitive impairment caused by substance abuse and HIV may contribute to increased HIV risk behavior. Impairment in cognitive function may hinder their rational decision-making and ability to practice safe drug- and sex-related choices (Anand et al., 2010). A longitudinal study conducted by Stacy et al. demonstrated that implicit cognition - referring to the learning, memory, and performance processes which take place without the participants' conscious awareness - was an independent predictor of unprotected sex in a high-risk sample. Even, after controlling other potential strong predictors (e.g., drug use, sensation seeking), implicit cognition remained a significant predictor of unprotected sex (Stacy et al., 2000) Some recent studies, aimed to determine the effects of impaired cognitive functioning on increased HIV risk behaviors among HIV negative drug offenders showed that higher working memory

and affective decision making capacity positively influenced condom use (Ames, Grenard, & Stacy, 2013; Grenard, Ames, & Stacy, 2013). In one study conducted by Grenard et al., working memory capacity served as a moderator in the relationship between spontaneous safe sex-related associations and condom use. Accessibility of spontaneous safe sex-related associations significantly predicted higher condom use among participants with greater working memory capacity (Grenard et al., 2013). Another study conducted by the same group of authors also showed that affective decision making ability interacted with spontaneous safe sex-related associations to predict condom use – higher the affective decision making ability, greater the condom use (Ames et al., 2013). Moreover, a study conducted by Mitchell et al., examining the relationship between cognitive functioning and both drug- and sex-related HIV risk behaviors among a sample of 229 injection drug users (IDUs) of heroin found that lower cognitive function predicted higher HIV risk behavior (both drug- and sex-related) (Mitchell et al., 2007). Studies proved that cognitive impairment is a high risk factor for HIV risk behaviors. Impairment of cognitive functioning is not only exhibited among HIV infected individuals, but also a very common phenomena among HIV negative drug users. Cognitive domains that are commonly impaired in drug users are attention, memory, and learning (Indlekofer et al., 2009; Lundqvist, 2005).

2.5 NCI and Self-efficacy

At a fundamental level, self-efficacy provides a perceived baseline by which people plan their future behaviors. All forms of psychotherapy and behavioral change operate through altering an individual's expectations of personal mastery and success – proposed by self-efficacy theory (Bandura, 1978). According to Bandura, two forms of expectancies - outcome

expectancies (the belief that certain behaviors will lead to certain outcomes), and self-efficacy expectancy (the belief that one can successfully perform the behavior in question) exhibit a strong impact on behavior (Bandura, 1978). Self-efficacy expectancy is a more potent predictor of behavior change, as it regulates the initial decision-making to perform a behavior, the effort expended, and the persistence in any adverse situation (Bandura, 1978). Recognition of the influence of self-efficacy on human behavior will lead to better understanding of the mechanism of behavior change (Bandura, 1978). In addition, research on understanding the impact of self-efficacy may have implications for adjusting intervention procedures to achieve desirable outcomes.

On the other hand, prior research has suggested an indirect effect of NCI on treatment outcomes (Meade, Conn, Skalski, & Safren, 2011; Pabst, Kraus, Piontek, Mueller, & Demmel, 2014). It thus may be beneficial to study the impact of NCI on treatment outcomes within more complex models that examine mediation and moderation relationships between NCI and one of the most powerful predictors of behavior change, self-efficacy. To date, very few studies have examined the interaction effect of NCI and self-efficacy on treatment outcomes. We have found only one study conducted by Worley et al. (2014) that examined the effects of NCI on substance abuse treatment outcomes (drinking or drug use) via self-efficacy among a sample of veterans. Greater NCI indirectly predicted poorer treatment outcomes via lower self-efficacy (i.e., confidence to resist use of alcohol or drugs across a variety of high-risk situations) (Worley et al., 2014). Thus, there has been very little investigation of the interaction of these particular variables and their impact on various treatment outcomes.

2.6 Self-efficacy and HIV Risk Behavior

Self-efficacy is a strong predictor of risk taking behaviors and treatment outcome (Bandura, 1990; Burleson & Kaminer, 2005). The lower the perceived self-efficacy, the higher the likelihood of engagement in high risk behaviors. Translating health information into effective self-protection action against risk taking behaviors requires a sense of personal power to exercise control over situations which depends on skills and self-efficacy (Bandura, 1990). In HIV risk reduction intervention, information, motivation, and behavioral skills and self-efficacy are the key determinants of HIV risk reduction behavior (M. M. Copenhaver & Lee, 2006).

Studies showed that lower self-efficacy significantly predicted higher levels of HIV risk behaviors (Bedoya et al., 2012; Nehl et al., 2015; Puffer et al., 2011; Thomas et al., 2009; Winningham et al., 2004). A mediational study conducted by Miner et al., examined the relationship between norms for condom use and unsafe sex (unprotected sex) via condom use self-efficacy in a sample of HIV infected MSM (Miner et al., 2009). They stated norms for condom use indirectly influenced unsafe sex through condom use self-efficacy in this sample. They suggested researchers should consider the impact of condom use self-efficay on risk behavior and intervenion should be designed to improve self-efficay (Miner et al., 2009). A very recent study conducted by Pitpitan et al., aimed to test the mechanism of injection risk intervention – how the intervention was reducing receptive needle sharing among female sex workers who inject drugs (FSWs-IDUs) in Mexico by moderated mediational analysis (Pitpitan et al., 2015). They showed that the intervention affected receptive needle sharing through safe injection self-efficacy in this population – those who had more safe injection self-efficacy were less likely to engage in needle sharing (Pitpitan et al., 2015). Studies documented that self-

efficacy influenced HIV risk behavior (unprotected sex and needle sharing) both directly and indirectly.

2.7 Gender Difference in NCI, Self-efficacy, and HIV Risk Behavior

Gender is another construct that plays a significant role in both self-efficacy and HIV risk behavior (Buchanan et al., 2006; Copenhaver, Lee, & Baldwin, 2013; Corsi et al., 2014; Lee, Salman, & Cooksey-James, 2016; Puffer et al., 2011; Stevens, Murphy, & McKnight, 2003; Zandmomen et al., 2014). Additionally, some studies report greater NCI in women than men (Gandhi et al., 2010; Royal et al., 2016; Shrestha et al., 2015; Troncoso & Conterno, 2015).

A study conducted by Corsi et al., intended to address the gender difference in predictors of HIV status among PWID in Ukraine, reported higher self-efficacy in women than men, but documented HIV risk behavior, both risky injection and risky sexual behavior, were more common in women than men (Corsi et al., 2014). Another cross-sectional study by Zandmomen et al., conducted on 400 HIV infected patients in Iran, also stated that women demonstrated higher self-efficacy, but reported risky behavior was more in women as well (Zandmomen et al., 2014). On the other hand, a study by Puffer et al., reported more sexual risky behavior and less safe sex self-efficacy in men (Puffer et al., 2011).

CHAPTER 3 : Hypotheses and Objectives

1st Objective: To analyze the influence of NCI on HIV preventive behaviors via self-efficacy.

1st Hypothesis: The influence of NCI on HIV preventive behaviors will be mediated by self-efficacy.

2nd Objective: To analyze the moderation effect of gender on relationship of NCI and HIV preventive behaviors via self-efficacy.

2nd Hypothesis: The predicted mediation effect will be significantly moderated by gender.

CHAPTER 4 : Methods

4.1 Design

This is a secondary data analysis that included a sample of HIV-negative opioid dependent individuals who participated in a Community-Friendly Health Recovery Program (CHRP; see http://www.nrepp.samhsa.gov/ProgramProfile.aspx?id=11), a behavioral HIV-risk reduction intervention which was a randomized control trial designed to reduce HIV transmission risk behavior among this risk population (M. M. Copenhaver et al., 2013). CHRP is an abbreviated, manual-guided intervention strategy, based on the information–motivation–behavioral skills (IMB) model of health behavior change, and comprised of four 1-hour group sessions that address sex-and drug-related HIV risk behaviors among individuals with opioid use disorders (OUDs), enrolled in Methadone Maintenance Therapy (MMT). The active control condition also received same number of sessions as intervention condition, but the session content was comprised of information regarding methadone program services and policies as well as general health care information (e.g., community resources) relevant to opioid-dependent patients entering methadone therapy. The sessions were conducted by bachelor's

level facilitators. The results of the RCT have been previously published (M. M. Copenhaver et al., 2013).

4.2 Participants

The current study included 236 HIV-negative opioid-dependent individuals who participated in the CHRP study and completed a 3-month follow-up assessment at the APT Foundation, Inc., in New Haven, CT. The inclusion criteria for the participants were: (a) 18 years or older, (b) met DSM-V criteria for opioid dependence, (c) newly enrolled in MMT, (d) reported sex- and/or drug-related HIV transmission risk behaviors in the past 6 months, and (e) not actively suicidal, homicidal, or psychotic.

4.3 Procedures

The study protocol was approved by the Institutional Review Board (IRB) at the University of Connecticut, the Human Investigation Committee at Yale University, and received board approval from the APT Foundation MMP, Inc.

All patients enrolled in MMT were screened for eligibility within one week of receiving the first methadone dose. Patients who were willing to participate in the study and also met the inclusion criteria, were provided a verbal and written description of the study and were asked to sign an informed consent form prior to random assignment to either the control (n = 115) or intervention (n = 121) condition. Participants were reimbursed for the time required to complete the assessments. An audio computer-assisted self-interview (ACASI) that has demonstrated sound psychometric properties (M. M. Copenhaver & Lee, 2006; M. M. Copenhaver, Lee, & Margolin, 2007; Fisher et al., 2004) was used to asses participants. In this current study, baseline

NCI, post-intervention self-efficacy, and 3-month follow-up data regarding HIV prevention intervention outcomes were included in our path analyses in order to examine the associations among theoretical variables of interest.

4.4 Measures

Participants' demographic details (gender, age, ethnicity, education, language, marital status, and income) and NCI were recorded at baseline. Self-efficacy and HIV prevention behavioral outcomes were measured at baseline, post-intervention, and follow-up.

4.4.1 NCI Measures

Participant's neurocognitive status was evaluated by Brief Inventory of Neurocognitive Impairment (BINI) (M. Copenhaver, Shrestha, Wickersham, Weikum, & Altice, 2016). BINI is a brief, self-report measure of 57-items and 9-factors which demonstrated excellent overall reliability (α=0.97). It was developed as a rapid and convenient way to help elicit diagnostically relevant information about both generalized NCI which is labeled as "Global Impairment" and specific symptom areas (e.g., attention, memory, linguistic functioning, etc.). Factors include Global Impairment that measured by 22 items (e.g., "I have difficulty paying attention" and "I get lost easily"), Academic-related contained 8 items (e.g., "I count with my fingers" and "I have trouble learning new things"), Language-related had 5 items (e.g., "My words get mixed up"), Memory-related was made up of 4 items (e.g., "I have trouble remembering people's names"), Psychomotor/physical comprised of 5 items (e.g., "I am very clumsy"), Psychomotor/perceptual included 5 items (e.g., "I have trouble with the left side of my body"), Anger-related had 3 items (e.g., "I have urges to break and smash things"), Pain-associated contained 3 items (e.g., "I have severe headaches"), and Traumatic Head Injury-related had 2

items (e.g., “I have been knocked unconscious”). The reliability of the 9 factors ranged from excellent to good (by factor: F1 α=0.97; F2 α=0.89; F3 α=0.82; F4 α=0.76; F5 α=0.79; F6 α=0.75; F7 α=0.75; F8 α=0.74; F9 α=0.73).

4.4.2 Self-efficacy Measures

Self-efficacy related to HIV risk reduction was measured for drug- and sex-related risk reduction behaviors separately as safe injection self-efficacy (SISE) and safe sex self-efficacy (SSSE). To measure SISE, following items were used: (1) “How hard to abstain from injecting?”, and (2) “How hard to always clean needle with bleach if you shared?”, whereas SSSE was measured using two subsequent items: (1) “How hard to abstain from sex?”, and (2) “How hard to always use condoms?”. All of these four items were measured by using 5-point Likert scale (“0=Very hard to do”, “1=Fairly hard to do”, “2=Neither hard nor easy to do”, “3=Somewhat easy to do”, “4=Very easy to do”). The sum of two items assessing SISE was used to measure participant’s self-efficacy in drug-related risk reduction behavior and the sum of other two items assessing SSSE was used to measure self-efficacy in sex-related risk reduction behavior. Higher score indicated greater self-efficacy.

4.4.3 HIV Prevention Behavior Measures

Participants’ HIV preventive behaviors were assessed separately for drug- and sex-related measures. Drug-related outcome included the use of clean needle use (CNU) as measured by five items: (1) “Did you inject illicit drugs in the past 7 days?”, (2) “If you injected drugs last week, have you shared rinse water?”, (3) “If you injected drugs last week, have you shared a cooker?”, (4) “If you injected drugs last week, have you shared cotton?”, and (5) “Have you used unclean needle or syringe after someone else?”. Sex-related outcome included

condom use (CU) as measured by three items: (1) “Do you use condoms every time you have sex?” (2) “Have you had oral, anal, or vaginal sex without using a condom, or other latex protection in the past 6 months?”, and (3) “Do you inconsistently (sometimes or never) use condoms or other latex protection for vaginal sex?”. “Yes” and “No” responses were used for assessing all these items. The corresponding items were added to obtain the total score for each measures. Higher score specified to higher CNU and CU. A recent confirmatory factor analysis was conducted to define these items measuring CNU and CU (Huedo-Medina, Shrestha, & Copenhaver, 2016).

4.5 Data Analysis

Analyses were designed to test our two hypotheses: (1) the effects of NCI (Independent Variable: IV) on HIV risk reduction behavior (Dependent Variable: DV) will be mediated by self-efficacy related to HIV risk reduction behavior (Mediator: Me), and (2) this mediation effect will be moderated by gender (Moderator: Mo).

Data analysis was conducted as follows: (1) Normality test was conducted for DV. Both subjective tests (Histograms and Q-Q plots) and objective tests (Shapiro-Wilk, Kolmogorov-Smirnov, Cramer-von Mises and Anderson-Darling) were used to specify the for participants’ distribution of data. (2) All assumptions of regression (linearity, homoscedasticity, and normality of residuals) were checked. (3) Descriptive statistics were provided for demographics and variables of interest. (4) In order to test our first hypothesis, we conducted mediation analysis by following the approach proposed by Imai et al. (Imai, Keele, Tnigley, & Yamamoto, 2010). First, HIV risk reduction self-efficacy (Me) was regressed on NCI (IV). Subsequently, HIV risk reduction behavior (DV) was regressed on NCI (IV) and self-efficacy (Me) controlling

for covariates. Finally, we estimated the average causal mediation effect (ACME), average direct effect (ADE), total effect (TE), and proportion of direct effect mediated by using the 'mediation' package in R (Imai et al., 2010). We reported results from Quasi Bayesian analysis. (5) In order to test our second hypothesis, whether the mediation effect depends on the level of gender, we incorporated gender as a moderator in path a, b, and c´, and tested the moderated mediation model. A significant interaction effect of gender with IV/Me is indicative of a moderated mediation effect._Our preliminary mediation models controlled for participants' demographics (gender, age, ethnicity, education, language, marital status, and income), group, and baseline HV risk reduction behaviors (CNU/CU). Aside from Gender, Group and demographics were not significantly associated with 3-month follow-up CNU and CU. Thus, in our final mediation models, we only controlled for baseline HIV risk reduction behavior (CNU/CU) and Gender. Further, in the moderated mediation models, we integrated Gender as a moderator and controlled for baseline CNU/CU. There were no missing values in the summed scores of CNU and CU.

CHAPTER 5 : Results

5.1 Normality test

Normality test was carried out for both dependent variables (CNU and CU). We used subjective tests (Histograms and Q-Q plots) and as well as objective tests (Shapiro-Wilk, Kolmogorov-Smirnov, Cramer-von Mises and Anderson-Darling) to specify the distribution of our dependent variables. Histogram, Q-Q plot, and Tests for Normality for CNU showed that distribution was approximately normal. Along with Tests for Normality (Figure 5), bell-shaped Histogram provided support for normal distribution (Figure 6) and as well as Q-Q plot (Figure 7).

Tests for Normality				
Test	**Statistic**		**p Value**	
Shapiro-Wilk	**W**	0.510825	**Pr < W**	<0.0001
Kolmogorov-Smirnov	**D**	0.452929	**Pr > D**	<0.0100
Cramer-von Mises	**W-Sq**	10.92408	**Pr > W-Sq**	<0.0050
Anderson-Darling	**A-Sq**	49.64225	**Pr > A-Sq**	<0.0050

Figure 5: Tests for Normality of 3-Month Follow-up Clean Needle Use

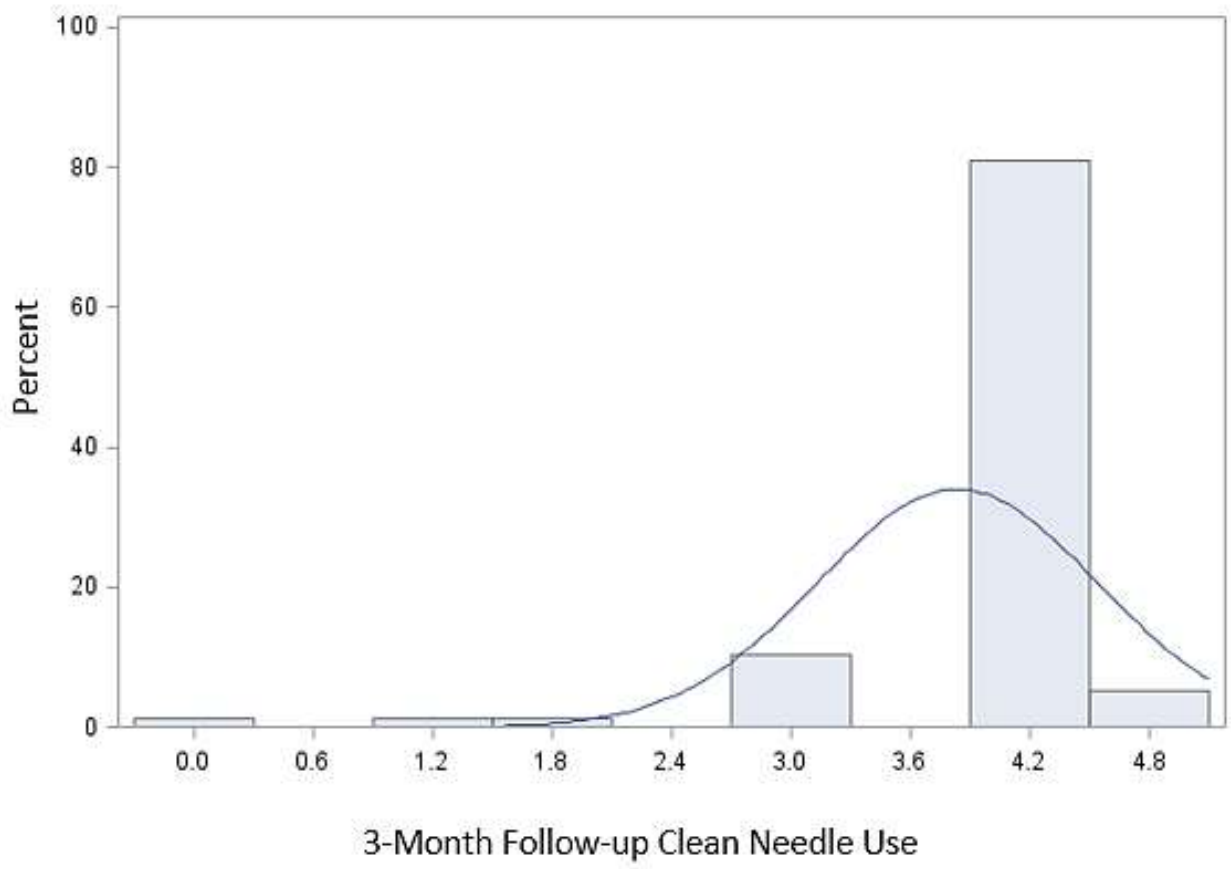

Figure 6: Histogram for 3-Month Follow-up Clean Needle Use

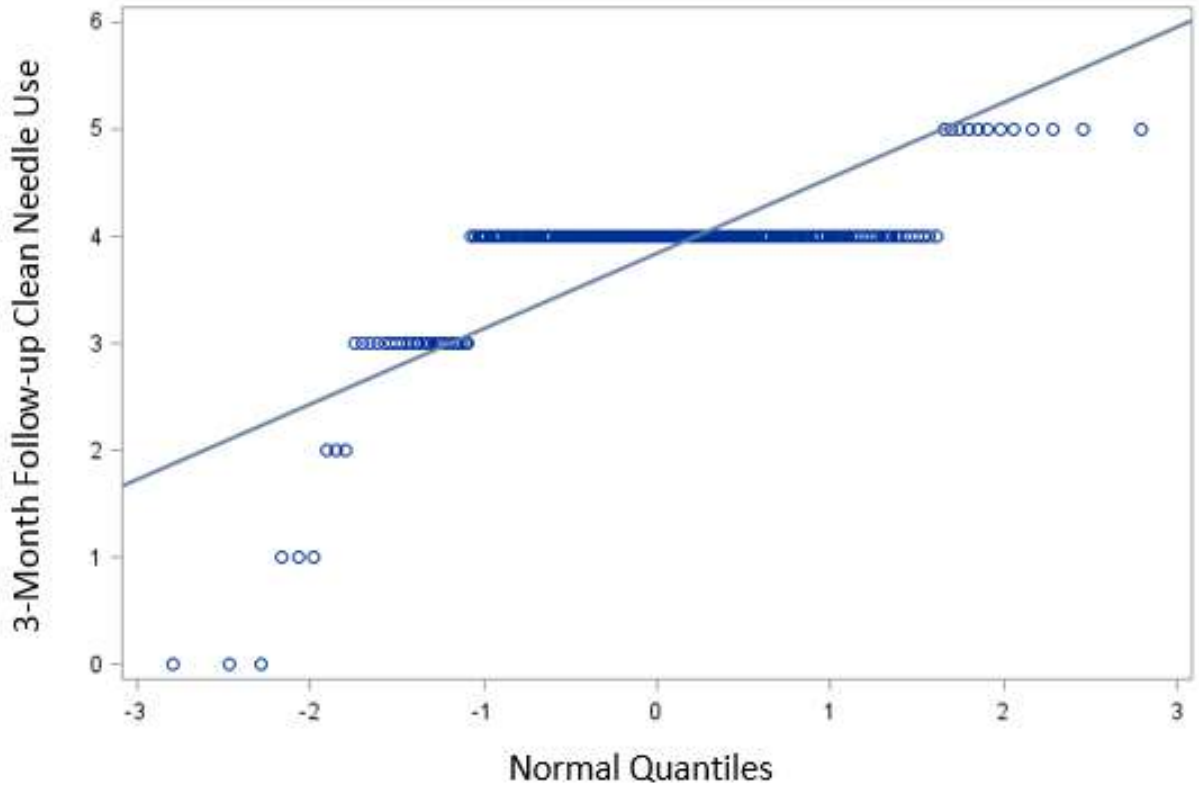

Figure 7: Q-Q Plot for 3-Month follow-up Clean Needle Use

Similarly, for CU, Tests for normality (Figure 8), bell-shaped Histogram (Figure 9), and Q-Q plot (Figure 10) demonstrated approximately normal distribution.

Tests for Normality				
Test	Statistic		p Value	
Shapiro-Wilk	W	0.751847	Pr < W	<0.0001
Kolmogorov-Smirnov	D	0.335245	Pr > D	<0.0100
Cramer-von Mises	W-Sq	4.27464	Pr > W-Sq	<0.0050
Anderson-Darling	A-Sq	25.78751	Pr > A-Sq	<0.0050

Figure 8: Tests for Normality of 3-Month Follow-up Condom Use

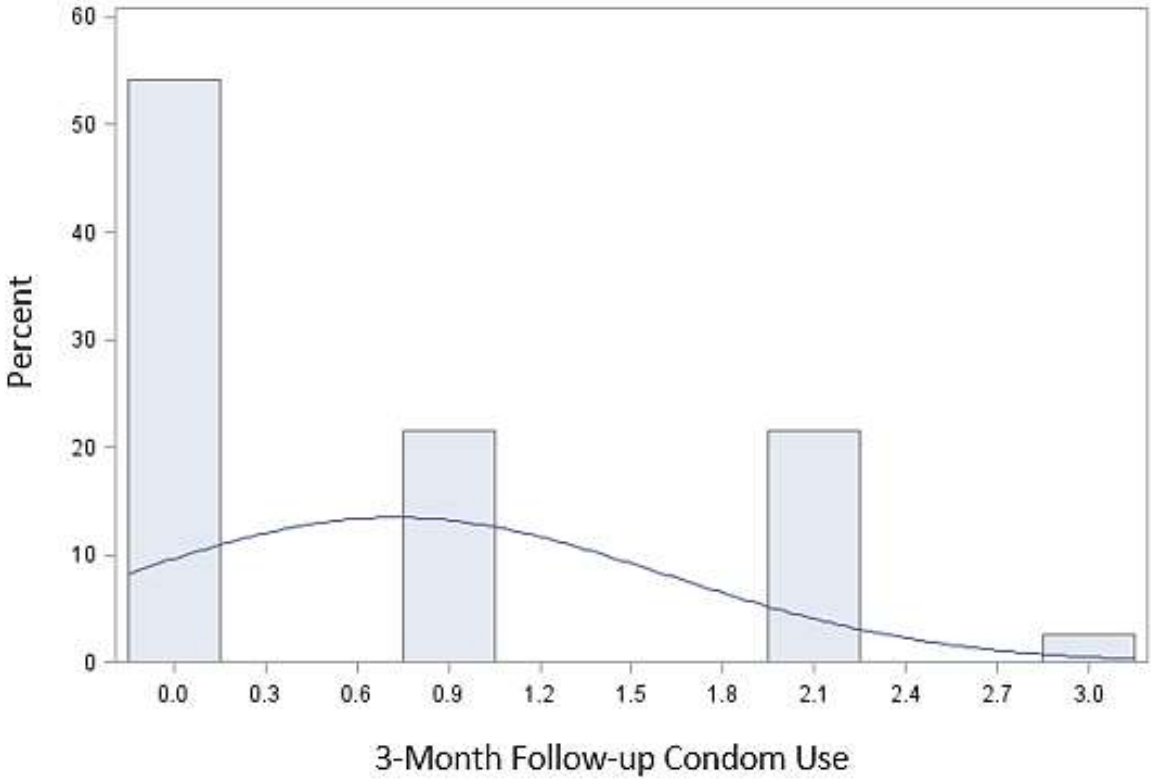

Figure 9: Histogram for 3-Month Follow-up Condom Use

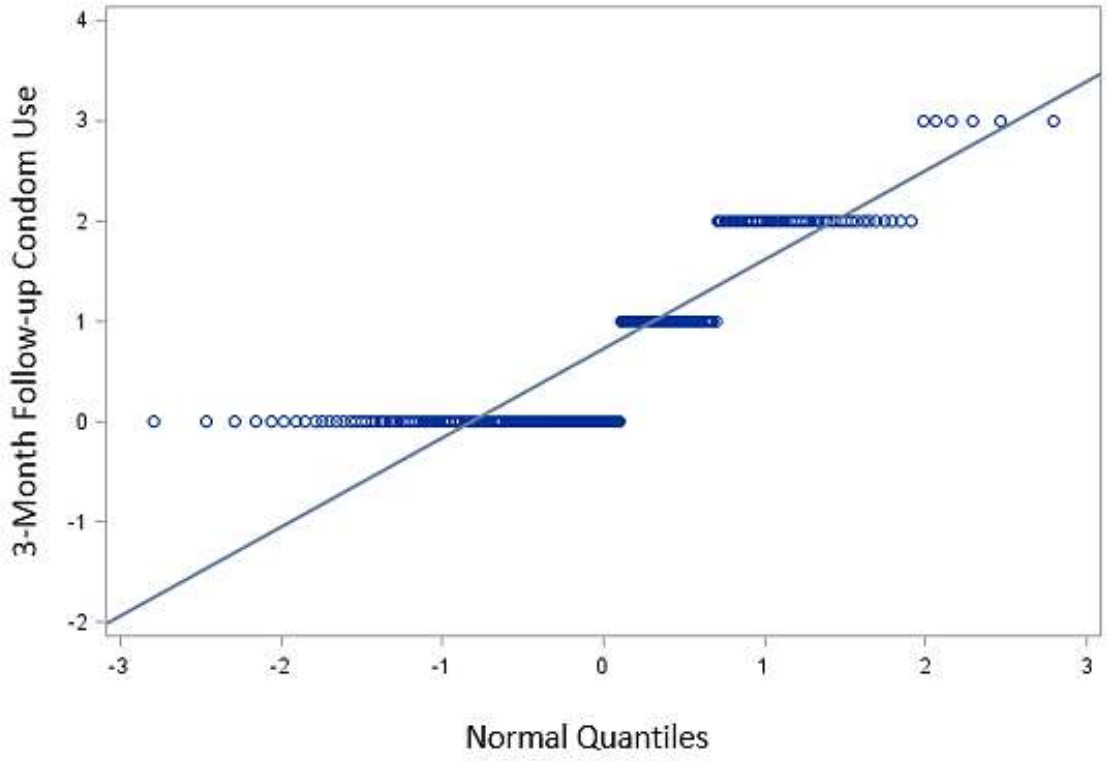

Figure 10: Q-Q Plot for 3-Month Follow-up Condom Use

5.2 Checking Assumptions of Regression

5.2.1 Linearity

Scatterplot did not indicate straight line linear relationship between IV (NCI) and DV (CNU/CU) (Figure 11, 13), and Me (SISE) and DV (CNU/CU) (Figure 12, 14).

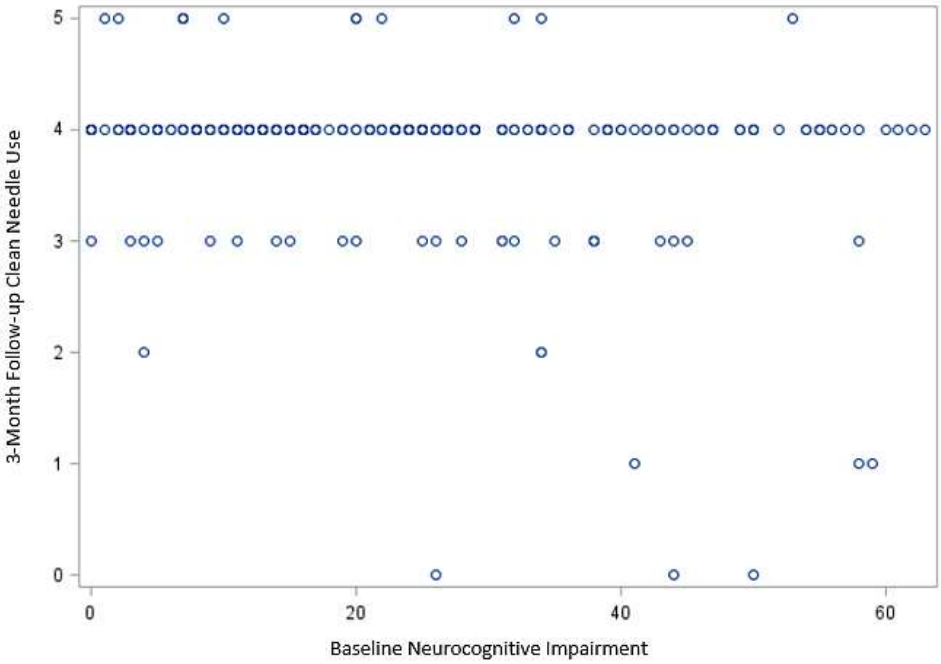

Figure 11: Scatterplot of 3-Month Follow-up Clean Needle use Vs Baseline Neurocognitive Impairment

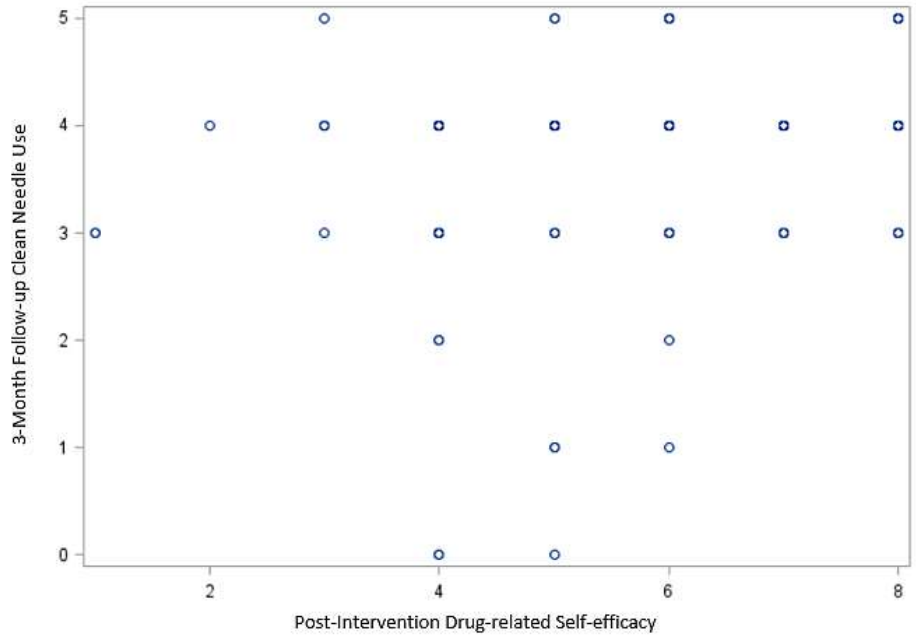

Figure 12: Scatterplot of 3-Month Follow-up Clean Needle use Vs Post-Intervention Sefe Injection Self-efficacy

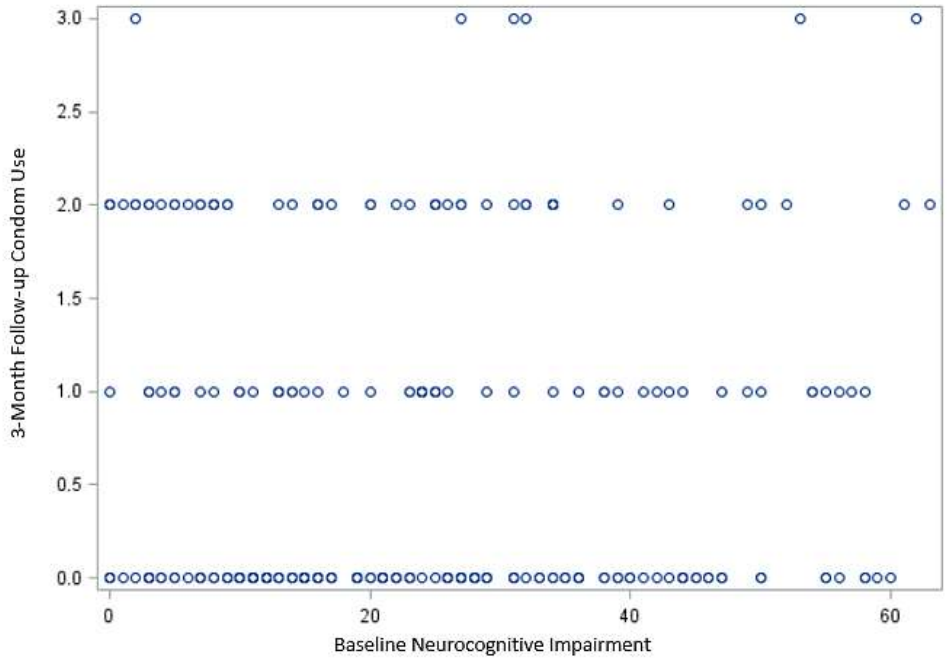

Figure 13: Scatterplot of 3-Month Follow-up Condom use Vs Baseline Neurocognitive Impairment

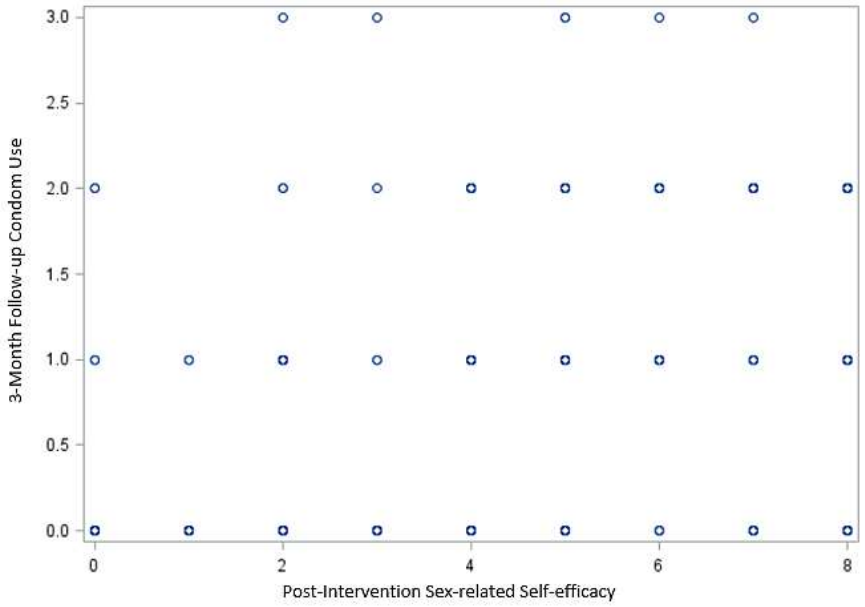

Figure 14: Scatterplot of 3-Month Follow-up Condom use Vs Post-Intervention Safe Sex Self-efficacy

5.2.2 Homoscedasticity of Residuals

Residuals for CNU (Figure 15, 16) and CU (Figure 17, 18) were randomly scattered around zero and studentized residuals did not create any pattern, which indicated constant variance.

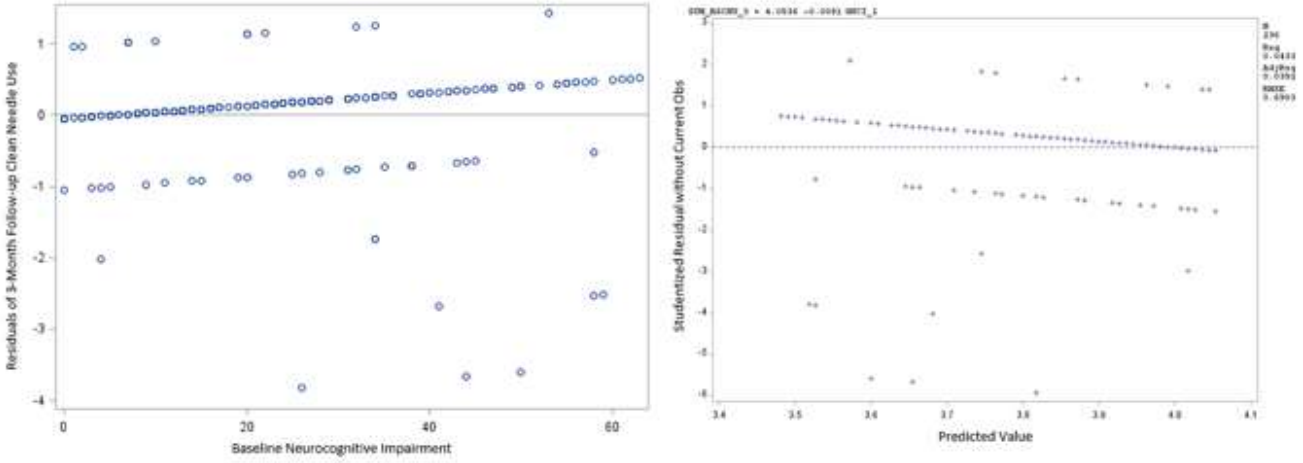

Figure 15: Plot of Residuals of 3-Month Follow-up Clean Needle Use (against Baseline Neurocognitive Impairment)

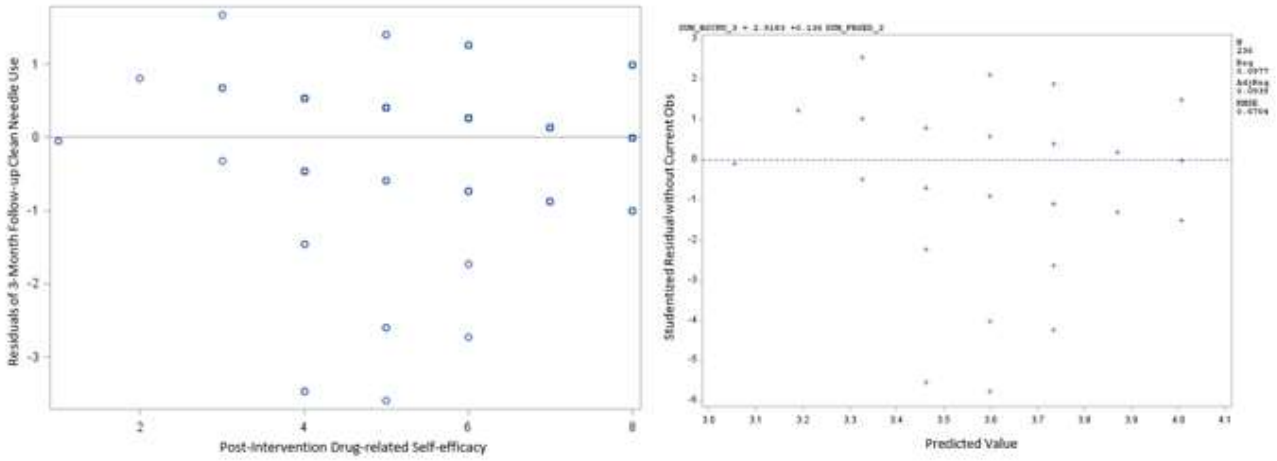

Figure 16: Plot of Residuals of 3-Month Follow-up Clean Needle Use (against Post-Intervention Safe Injection Self-efficacy)

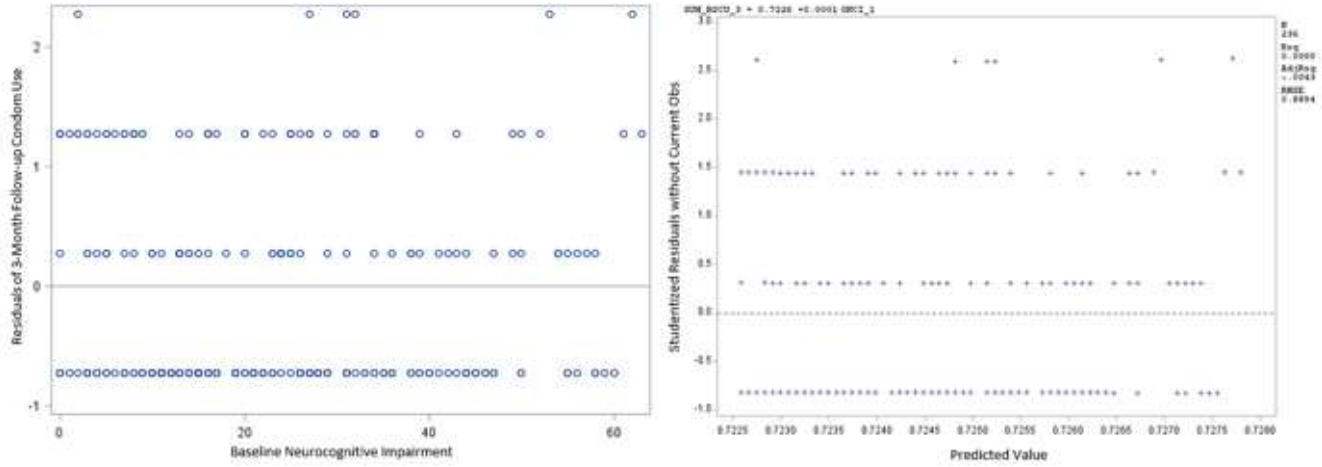

Figure 17: Plot of Residuals of 3-Month Follow-up Condom Use (against Baseline Neurocognitive Impairment)

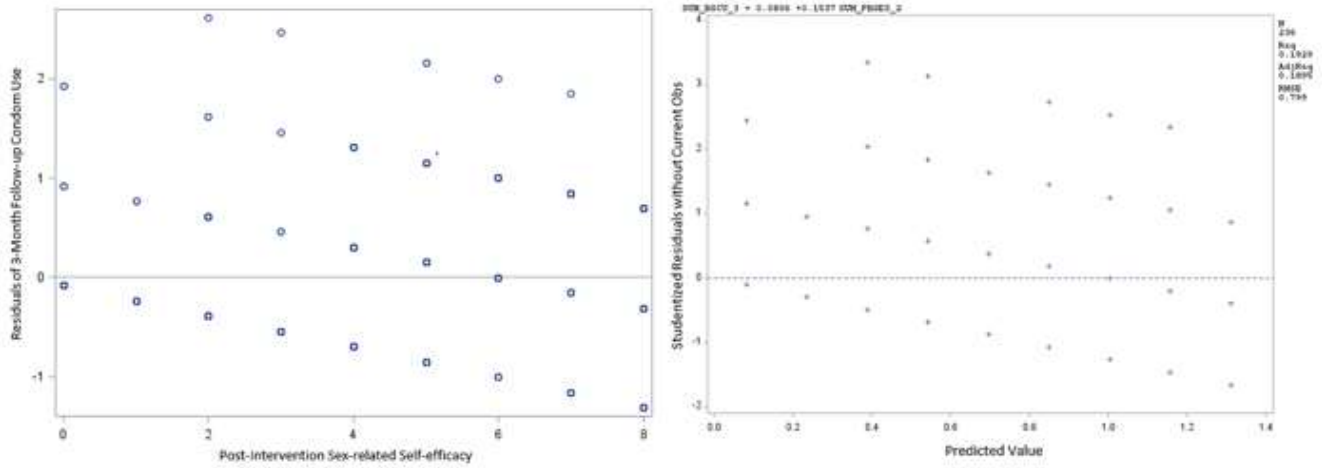

Figure 18: Plot of Residuals of 3-Month Follow-up Condom Use (against Post-Intervention Safe Sex Self-efficacy)

5.2.3 Normality of Residuals

Residuals for CNU (Figure 19, 20) and CU (Figure 21, 22) were normally distributed. Histograms for residuals of CNU (Figure 19) and CU (Figure 21) were Bell-shaped and in Q-Q plot there were not any definite curve (Figure 20, 22), though data were above and below the line which indicated skewness.

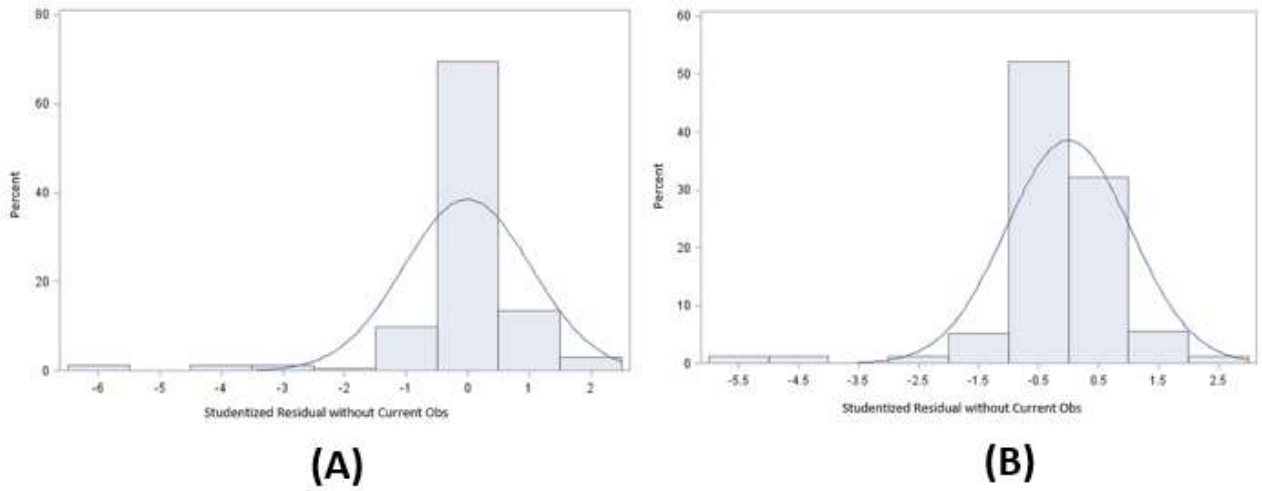

Figure 19: Histogram of Residuals of 3-Month Follow-up Clean Needle Use against (A) Baseline Neurocognitive Impairment (IV) & (B) Post-Intervention Safe Injection Self-efficacy (Me)

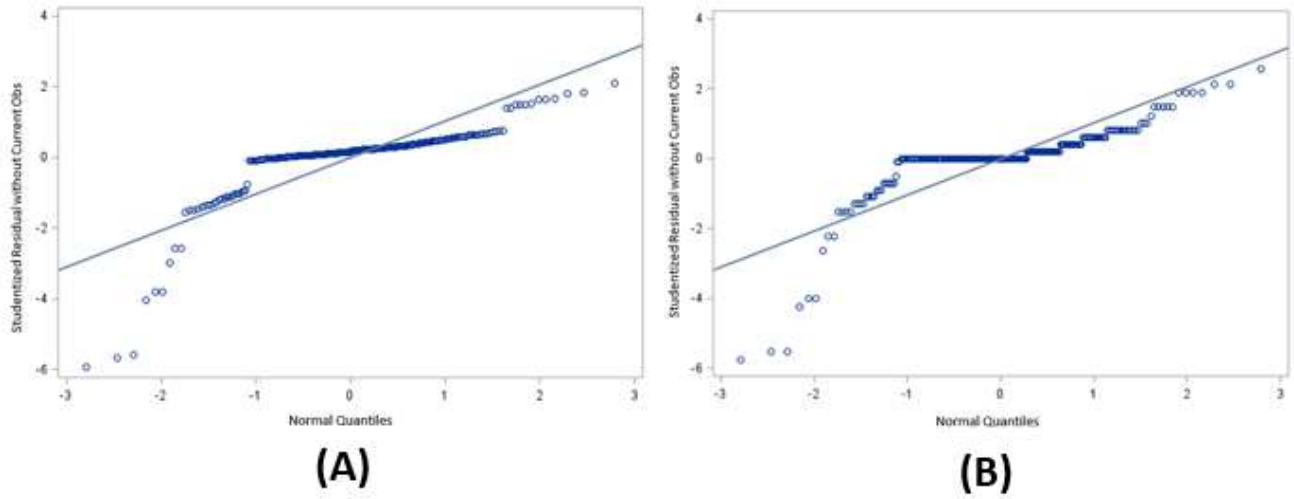

Figure 20: Q-Q Plot of Residuals of 3-Month Follow-up Clean Needle Use against (A) Baseline Neurocognitive Impairment (IV) & (B) Post-Intervention Safe Injection Self-efficacy (Me)

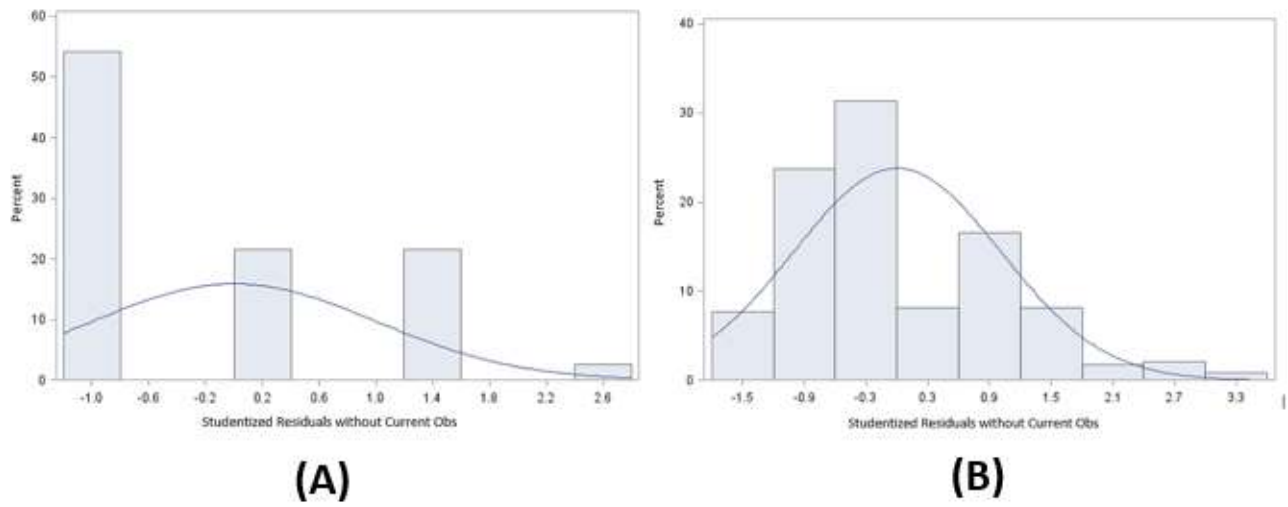

Figure 21: Histogram of Residuals of 3-Month Follow-up Condom Use against (A) Baseline Neurocognitive Impairment (IV) & (B) Post-Intervention Safe Sex Self-efficacy (Me)

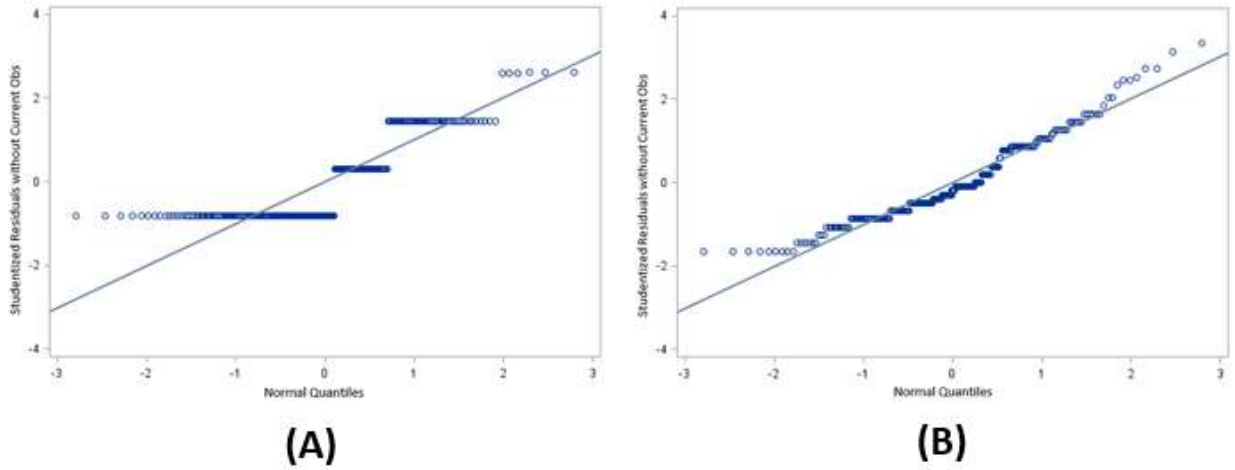

Figure 22: Q-Q Plot of Residuals of 3-Month Follow-up Condom Use against (A) Baseline Neurocognitive Impairment (IV) & (B) Post-Intervention Safe Sex Self-efficacy (Me)

5.3 Descriptive Statistics

Among all participants (n = 236, 108 males), a majority were Caucasian (73.73%), never married (66.1%), English-speaking (94.92 %), with 12 years of education (47.46%), annual income less than $11,000 (86.09%), and median age of 34 (Table 1). All participants had some degree of neurocognitive impairment (Figure 23). The mean scores of SISE, SSSE, CNU, and CU were 6.74 (±1.62), 4.19 (±2.54), 3.82(±0.70), and 0.72(±0.89), respectively (Table 2).

Table 1: Demographic characteristics of participants (*n* = 236)

Participants		Frequency	Percentage
Gender	Male	108	46
	Female	128	54
Ethnicity	White	174	73.73
	African American	23	9.75
	Hispanic / Latino	33	13.98
	Other	6	2.54
Years of Education	6 or below	4	1.69
	12 or below	112	47.46
	16 or below	8	3.39
	More than 16	2	0.85
Marital status	Married	22	9.32
	Never married	156	66.10
	Separated	19	8.05
	Divorced	35	14.83
	Widowed	4	1.69
Income	0 to $10,999	99	86.09
	$11,000 to $20,999	8	6.96
	$21,000 to $30,000	4	3.48
	Over $30,000	4	3.48
Language	English	224	94.92
	Spanish	12	5.08
Age	Median	34	

Table 2: Summary statistics of HIV risk reduction self-efficacy and behaviors

Participants	Variables	Mean	Std Dev	Min	Max
236	SISE	6.74	1.62	1	8
	SSSE	4.19	2.54	0	8
	CNU	3.83	0.70	0	5
	CU	0.72	0.89	0	3

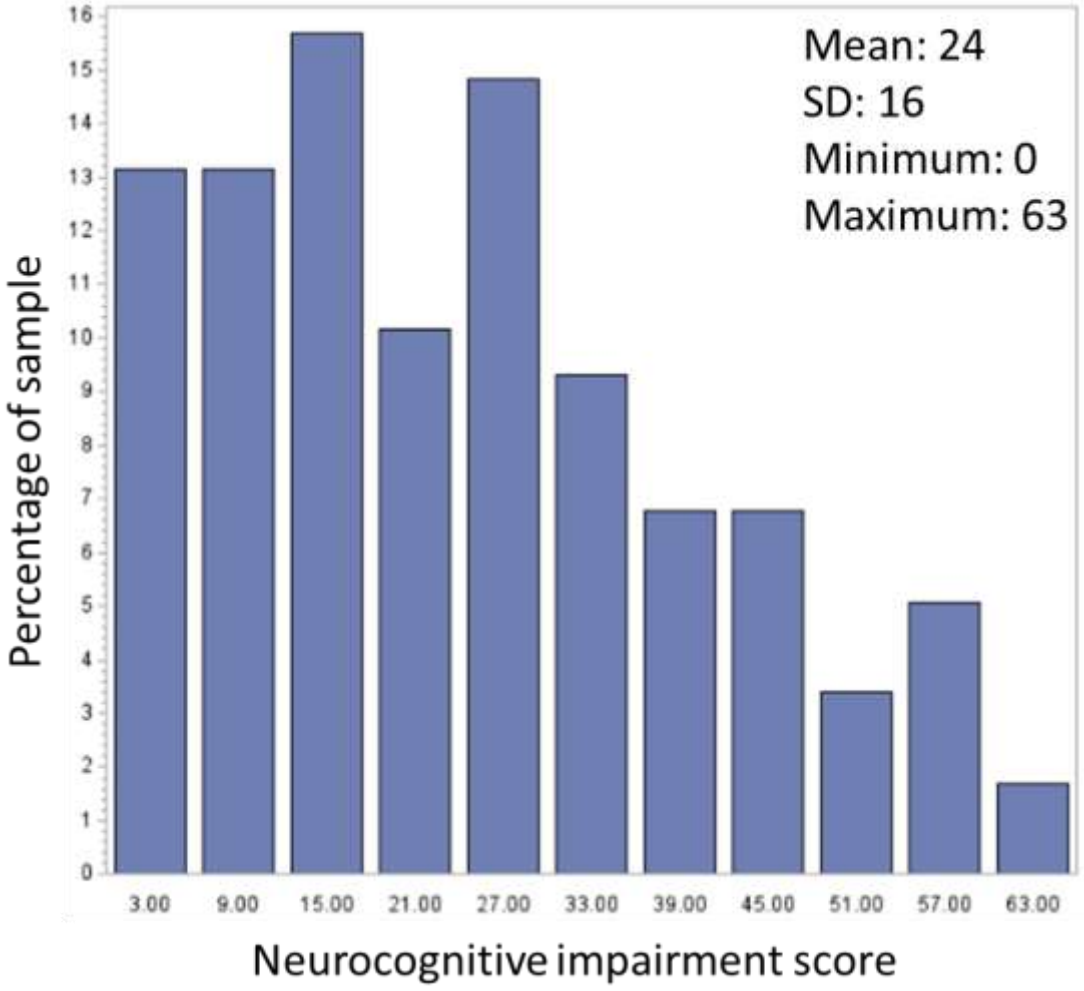

Figure 23: Prevalence of neurocognitive impairment

5.4 Mediation Test

In order to conduct mediation analysis following the rules of Baron and Kenny (Baron & Kenny, 1986), we first tested the effects of baseline NCI on 3-month follow-up HIV risk reduction behavior and post-intervention self-efficacy to examine whether the predictor (baseline NCI) was significantly associated with the outcome (3-month follow-up CNU/CU) and mediator (post-intervention SISE/SSSE). Higher NCI significantly predicted lower CNU (β = -0.006, p = 0.03), but not CU (β = -0.0008, p = 0.81). Higher NCI also significantly predicted lower SISE (β = -0.016, p = 0.016) and lower SSSE (β = -0.023, p = 0.024). After establishing the relationship between predictor and mediator, we examined whether the mediator predicted future outcome. SISE and SSSE were tested separately as predictor of CNU and CU, controlling for predictor (NCI) and covariates (Baseline CNU/CU and gender). Greater SISE and SSSE significantly predicted higher future CNU (β = 0.098, $p < 0.001$) and CU (β = 0.137, $p < 0.001$), respectively. With these results providing reasonable support for mediation, we conducted causal mediation analyses (using 'mediation' package) and estimated ACME, ADE, and TE for both CNU model and CU model (Imai et al., 2010).

For the CNU model, where we controlled for baseline CNU and gender, (Figure 24), ACME was significant, the effect of NCI on CNU was significantly mediated by SISE (β= -0.0016, CI [-0.003, -0.0003], p= 0.02, proportion of direct effect mediated 25%). The direction of relationship between NCI and SISE (β=-0.016, p=0.01), and the relationship between SISE and CNU (β=0.098, $p<0.001$) indicated that greater NCI predicted lower SISE, and lower SISE, in turn, predicted lower future CNU (at follow-up). The ADE of NCI on CNU (controlling for SISE) was not significant (β= -0.004, CI [-0.009, 0.001], p= 0.13), but the TE of NCI on CNU was significant (β= -0.006, CI [-0.01, -0.0004], p= 0.03). The estimate of total effect (β= -0.006)

was larger than the estimate of direct effect (β=-0.004) and also the direct effect was not significant, but the total effect was significant – which establishes complete mediation (Baron & Kenny, 1986).

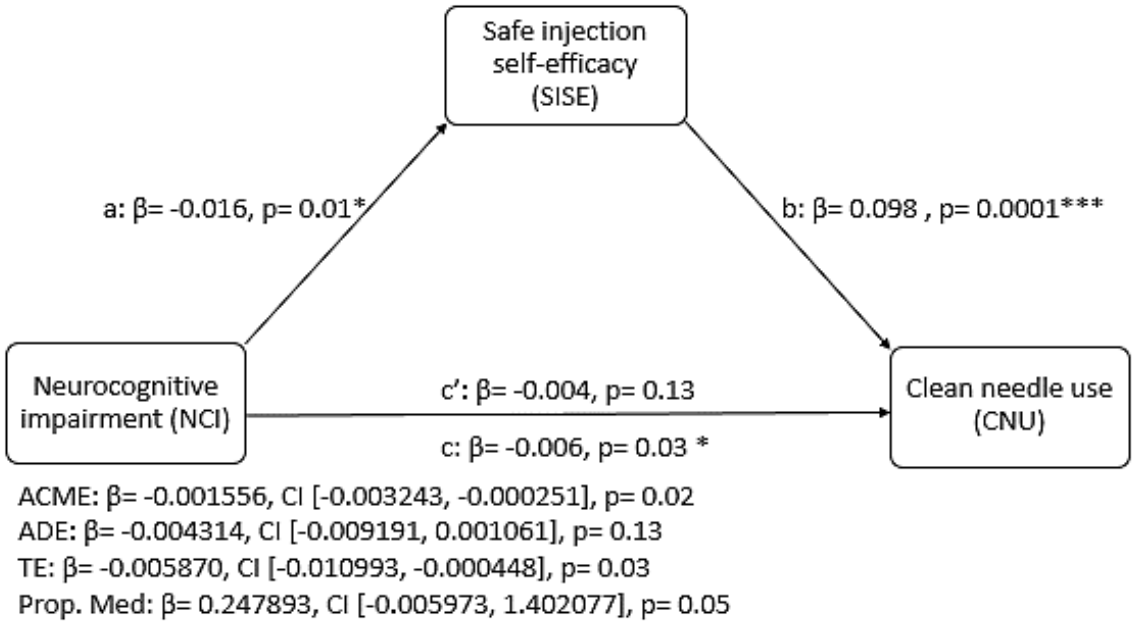

Figure 24: Causal mediation analysis – Clean Needle Use (CNU) Model

Similarly, ACME was significant for CU model, controlling for baseline CU and gender (Figure 25), the effect of NCI on CU was also significantly mediated by SSSE (β= -0.003, CI [-0.006, -0.0004] p= 0.02, proportion of direct effect mediated 59%). The estimates of NCI and SSSE (β=-0.023, p=0.02), and SSSE and CU (β=0.137, p<0.001) showed that greater NCI also predicted lower SSSE, and lower SSSE, in turn, predicted lower future CU. Both TE of NCI on CU (β= -0.0008, CI [-0.007, 0.006], p= 0.81) and ADE of NCI on CU (controlling for SSSE) (β= 0.002, CI [-0.003, 0.009], p= 0.47) were not significant and the direction of direct effect

(β= 0.002) was opposite to the direction of indirect effect (β= -0.003) – which suggests inconsistent mediation (David P. MacKinnon, Fairchild, & Fritz, 2007).

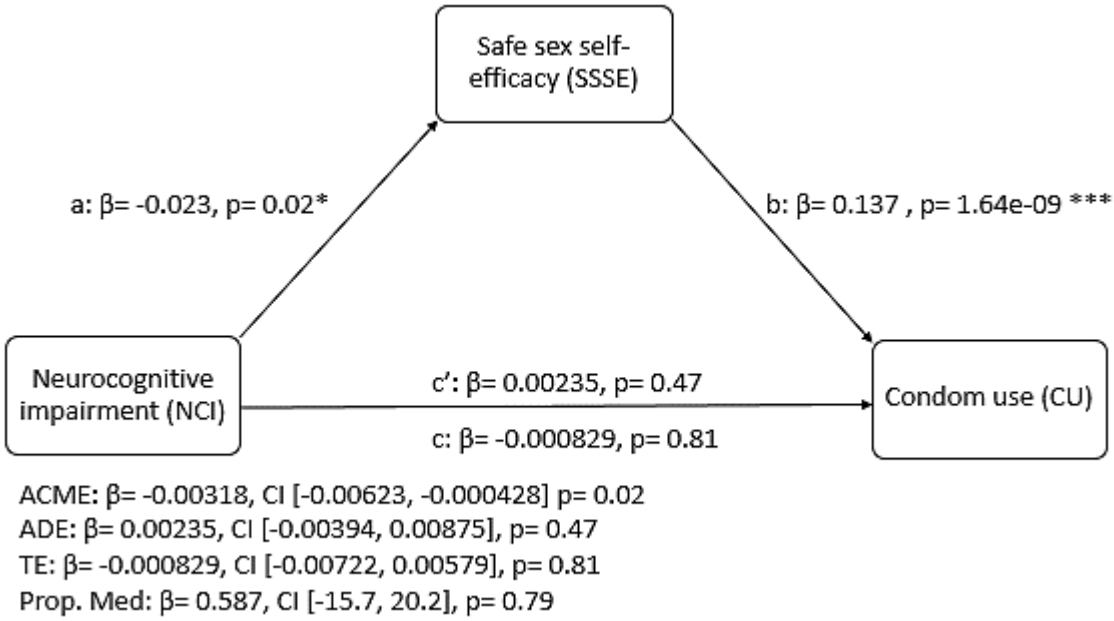

Figure 25: Causal mediation analysis - Condom Use (CU) Model

5.5 Moderated Mediation Test

In order to test our second hypothesis, that the indirect effects of NCI on HIV risk reduction behavior via self-efficacy would be significantly moderated by gender, we examined the moderation effect of gender on the relationship between NCI and self-efficacy, and also on the relationship between self-efficacy and HV risk reduction behavior.

For the CNU model, gender moderated both path b and c´, the relationship between SISE and CNU, and the relationship between NCI and CNU, respectively. The interaction effects between gender and SISE (β= 0.092, p= 0.06), and gender and NCI (β= 0.01, p= 0.06) were slightly significant. Given that this result provided support for moderated mediation, we

estimated ACME for males and females separately, and the mediation effect was significant for females (β= -0.002, CI [-0.005, 0.00001], p= 0.06, proportion of direct effect mediated 47%). Though the p-value was only marginally significant and the CI contains zero, the proportion of direct effect of NCI on CNU mediated by SISE was significant (47%).

For the CU model, we did not find any significant interaction effect regarding gender. As, gender was a significant moderator in our CNU model and previous studies, we estimated ACME for males and females separately; however, we did find a significant mediation effect for females (β= -0.006, CI [-0.012, -0.002], p= 0.00, proportion of direct effect mediated 80%).

CHAPTER 6 : Discussion

In our sample, self-efficacy mediated the relationship of NCI on HIV risk reduction behaviors for both clean needle use and condom use, and these mediation effects were significant only for females. This is the first study to date to explore the complex relationship of NCI, self-efficacy, gender, and HIV risk reduction behavior among OUDs within a treatment setting. Our study developed a theoretical framework that establish a mediation effect of self-efficacy in the relationship between NCI and key HIV risk reduction behaviors (e.g., clean needle use and condom use) that varied significantly as a function of gender.

The results of the CNU model demonstrated that participants' greater drug-related HIV risk reduction behavior (i.e., clean needle use) was predicted by lower NCI, and this relationship was completely mediated by their HIV risk reduction self-efficacy (i.e., safe injection self-efficacy), as the direct effect was not significant, but the total effect was significant. The effect of NCI on CNU was going directly through SISE – with lower NCI predicting higher SISE, and higher SISE predicting greater CNU.

When we examined the CU model, the effect of NCI on HIV risk reduction behavior (i.e., condom use) was inconsistently mediated by HIV risk reduction self-efficacy (i.e., safe

sex self-efficacy), as both the direct effect and the total effect were not significant. In this case, lower NCI did not predict greater CU, but rather predicted higher SSSE, and higher SSSE predicted greater CU. We note, however, inconsistent mediation does not indicate an absence of significant findings; rather, it indicates mediation which occurs in the absence of a significant total effect and direct effect when the mediator functions as a suppressor variable or in the context of undetected moderator effects (David Peter MacKinnon, 2008). We also note that prior research has shown a similar pattern of inconsistent mediation effects of self-efficacy on substance use outcomes as well (Worley et al., 2014).

In this study, the mediation effects of self-efficacy for both clean needle use and condom use models were moderated by gender (only for females). Thus, gender moderated the relationship between self-efficacy and HIV risk reduction behavior.

Overall, the results are consistent with previous research – lower neurocognitive impairment was shown to be associated with higher self-efficacy (Bates, Pawlak, Tonigan, & Buckman, 2006; Worley et al., 2014) and lower HIV risk reduction behaviors (Ezeabogu et al., 2012; Gonzalez et al., 2005; Schuster, Crane, Mermelstein, & Gonzalez, 2012; Shrestha & Copenhaver, 2016). Prior studies also predicted greater self-efficacy to be associated with higher HIV risk reduction behavior (Bedoya et al., 2012; Nehl et al., 2015; Puffer et al., 2011; Thomas et al., 2009). Interestingly, we found a significant mediation effect of self-efficacy in the relationship between neurocognitive impairment and HIV risk reduction behaviors, only in females. This results show that self-efficacy is a significant predictor of HIV risk reduction behaviors for female drug users, which is supported by previous research where females were more likely than males to respond with improvement in self-efficacy (Corsi et al., 2014).

Taken together, the results indicate the need for future studies to develop and test intervention strategies that better accommodate the effects of NCI on key intervention outcomes including self-efficacy, particularly for female participants. Many interventions target both genders at the same time without considering specific behavioral components (e.g., self-efficacy) and cognitive status (e.g., NCI). However, previous research has shown that interventions are more effective when targeting high risk populations, a specific gender (either men or women), and behavioral components/skills training (Crepaz et al., 2006; Huedo-Medina et al., 2010; Scott-Sheldon, Huedo-Medina, Warren, Johnson, & Carey, 2011; Tan, Huedo-Medina, Warren, Carey, & Johnson, 2012). The positive association between self-efficacy and HIV risk reduction behavior in our study underlines the need to address self-efficacy to improve HIV risk reduction, particularly in the programs those geared toward female drug users. Information or skills that can enhance self-efficacy of condom use and clean needle use may be essential to be included in order to have an effective HIV prevention intervention program. Better accommodation of the effects of NCI by repeating the information and skills, and a gender-specific intervention that aims to improve self-efficacy could positively influence HIV risk reduction behavior, such as clean needle use and condom use.

This current study has several limitations. Firstly, the study was conducted in a drug treatment setting among drug users which restricts our ability to generalize the findings to other risk populations, such as non-drug involved populations, non-treatment settings, or to persons not meeting our inclusion criteria including a readiness to participate. In addition, the majority of the sample was Caucasian, and that also limits the generalizability of our results to more ethnically diverse populations. Secondly, as the participants were newly enrolled individuals in a methadone maintenance drug treatment facility, the risk reduction effects that methadone

exerts on drug use and related HIV risk behaviors (Amato et al., 2013; Maremmani, Pani, Pacini, & Perugi, 2007; Otiashvili et al., 2013; Shi et al., 2007) may have influenced the effects of mediators and moderators on the HIV risk reduction outcomes. Thirdly, we did not include behavior skills in our analysis, although, theoretically, skills are sometimes included in the measurement of self-efficacy. Finally, all assessments were based on self-report in the primary RCT study which carries with it inherent limitations due to participants' possible reluctance to self-report socially unacceptable behaviors (Turner, Rogers, Hendershot, Miller, & Thornberry, 1996). This might have been reduced, however, by the use of ACASI (Audio Computer Assisted Self-Interview) system, which allowed participants to respond with a high level of privacy.

CHAPTER 7 : Summary & Future Directions

Understanding how cognitive impairment impact drug- and sex-related HIV risk reduction behaviors is essential to reduce HIV risk effectively (Anand et al., 2010). The current study provides preliminary evidence that neurocognitive impairment adversely impacts drug- and sex-related HIV risk reduction outcomes through the mediating variable of self-efficacy. Previous research showed that cognitive deficits influence HIV risk behaviors among drug users, as the cognitive domains that are affected in drug users are essential to acquire, retain, and utilize HIV preventive behaviors (M. Copenhaver, Avants, Warburton, & Margolin, 2011). It is important to develop a treatment strategy where we can accommodate cognitive impairment to prevent HIV risk behaviors for this population. Multimodal presentation of material (e.g., verbally, visually, and experimentally) is a very effective way for the cognitively impaired participants to retain information and skills. In the parent study, during the group sessions, information was provided both verbally and visually. Participants were encouraged to engage in treatment process by asking questions. Additionally, during teaching the risk reduction behaviors skills, the proper procedure of cleaning the injection equipment and the proper application of condom by using a penis replica were demonstrated by showing video

clips. Participants also practiced these risk reduction skills during the sessions which helped them to retain the information and skills. Visual, verbal, and experimental presentation of materials increases concentration and aids to avoid fatigue in cognitively impaired populations who get tired easily. Moreover, frequent review of materials helped with the retention of information, building confidence, and skills. To develop an appropriate treatment strategy, it is essential to identify when cognitive impairment may impact full participation. We did not set a diagnostic cut point when we measured NCI in this study, but doing so in future work could be beneficial to help clinicians identify when NCI is a significant barrier for HIV treatment/ prevention. Thus, it was not the focus of the present study, but should be addressed in future studies aimed at better screening and accommodating NCI.

Moreover, previous studies have demonstrated that evidence based interventions (EBI) incorporating cognitive remediation strategies - with an emphasis on practical applications (e.g. motivation, self-efficacy, skills and role-play) - are the most effective at reducing risk among cognitively impaired populations (Kalichman, 2008). In this current study, we found that self-efficacy predicted HIV risk reduction behavior significantly and, furthermore, self-efficacy was predicted by NCI. Overall, self-efficacy significantly mediated the relationship between NCI and HIV risk reduction behavior. In addition, the mediation effect of self-efficacy was moderated by gender and the mediation was significant only for women in this sample of PWUDs, which indicates the need of future studies aiming to improve self-efficacy, particularly for female drug users with neurocognitive impairment to reduce HIV risk behaviors. Recent work indicates that the pattern of cognitive difficulties, like, impairment in memory, information processing, and decision making in drug users may be addressed in future interventions by incorporating mHealth (mobile health) or Pre-Exposure Prophylaxis (PrEP).

Recognizing and understanding these components, and tailoring interventions accordingly seems to be essential in order to optimize intervention approaches that targeting this population.

REFERENCES

Amato, L., Davoli, M., Minozzi, S., Ferroni, E., Ali, R., & Ferri, M. (2013). Methadone at tapered doses for the management of opioid withdrawal. *The Cochrane Database of Systematic Reviews*, *2*, CD003409. http://doi.org/10.1002/14651858.CD003409.pub4

Ames, S. L., Grenard, J. L., & Stacy, A. W. (2013). Dual process interaction model of HIV-risk behaviors among drug offenders. *AIDS and Behavior*, *17*(3), 914–925. http://doi.org/10.1007/s10461-012-0140-2

Anand, P., Springer, S. a, Copenhaver, M. M., & Altice, F. L. (2010). Neurocognitive impairment and HIV risk factors: a reciprocal relationship. *AIDS and Behavior*, *14*(6), 1213–1226. http://doi.org/10.1007/s10461-010-9684-1

Antinori, A., Arendt, G., Becker, J. T., Brew, B. J., Byrd, D. A., Cherner, M., … Wojna, V. E. (2007). Updated research nosology for HIV-associated neurocognitive disorders. *Neurology*, *69*(18), 1789–1799. http://doi.org/10.1212/01.WNL.0000287431.88658.8b

Arasteh, K., Des Jarlais, D. C., & Perlis, T. E. (2008). Alcohol and HIV sexual risk behaviors among injection drug users. *Drug and Alcohol Dependence*, *95*(1-2), 54–61. http://doi.org/10.1016/j.drugalcdep.2007.12.008

Bandura, A. (1978). Self-efficacy: Toward a unifying theory of behavioral change. *Advances in Behaviour Research and Therapy*, *1*(4), 139–161. http://doi.org/10.1016/0146-6402(78)90002-4

Bandura, A. (1990). Perceived self-efficacy in the exercise of control over AIDS infection. *Evaluation and Program Planning*, *13*(1), 9–17. http://doi.org/10.1016/0149-7189(90)90004-G

Baron, R. M., & Kenny, D. a. (1986). The Moderator-Mediator Variable Distinction in Social Psychological Research: Conceptual, Strategic, and Statistical Considerations. *Journal of Personality and Social Psychology*, *51*(6), 1173–1182. http://doi.org/10.1037/0022-3514.51.6.1173

Bates, M. E., Pawlak, A. P., Tonigan, J. S., & Buckman, J. F. (2006). Cognitive impairment influences drinking outcome by altering therapeutic mechanisms of change. *Psychology of Addictive Behaviors : Journal of the Society of Psychologists in Addictive Behaviors*, *20*(3), 241–53. http://doi.org/10.1037/0893-164X.20.3.241

Bedoya, C. A., Mimiaga, M. J., Beauchamp, G., Donnell, D., Mayer, K. H., & Safren, S. A. (2012). Predictors of HIV transmission risk behavior and seroconversion among Latino men who have sex with men in Project EXPLORE. *AIDS and Behavior*, *16*(3), 608–17. http://doi.org/10.1007/s10461-011-9911-4

Buchanan, D., Tooze, J. A., Shaw, S., Kinzly, M., Heimer, R., & Singer, M. (2006). Demographic, HIV risk behavior, and health status characteristics of “crack” cocaine injectors compared to other injection drug users in three New England cities. *Drug and Alcohol Dependence*, *81*(3), 221–229. http://doi.org/10.1016/j.drugalcdep.2005.07.011

Burleson, J. a., & Kaminer, Y. (2005). Self-efficacy as a predictor of treatment outcome in adolescent substance use disorders. *Addictive Behaviors*, *30*(9), 1751–1764. http://doi.org/10.1016/j.addbeh.2005.07.006

CDC. (2010). Cognitive impairment: A Call for Action, Now! *The U.S. Department of Health and Human Services, Centers for Disease Control and Prevention*, 1–4.

CDC. (2015). HIV in the United State: At a glance. *CDC*, (July). http://doi.org/10.1016/j.socscimed.2006.09.015

Centers for Disease Control and Prevention. (2013). HIV and substance use in the United States. *CDC*, (March). Retrieved from http://www.cdc.gov/hiv/risk/behavior/substanceuse.html

Centers for Disease Control and Prevention. (2014). Centers for Disease Control and P. HIV Surveillance Report, 2012, *24*, 83.

Chiesi, A., Seeber, A. C., Dally, L. G., Floridia, M., Rezza, G., & Vella, S. (1996). AIDS dementia complex in the Italian National AIDS Registry: Temporal trends (1987-93) and differential incidence according to mode of transmission of HIV-1 infection. *Journal of the Neurological Sciences*, *144*(1-2), 107–113. http://doi.org/10.1016/S0022-510X(96)00192-X

Clifford, D. B., & Ances, B. M. (2013). HIV-associated neurocognitive disorder (HAND). *The Lancet. Infectious Diseases*, *13*(11), 976–986. http://doi.org/10.1016/S1473-3099(13)70269-X

Copenhaver, M., Avants, S. K., Warburton, L. A., & Margolin, A. (2011). Intervening effectively with drug abusers infected with HIV: taking into account the potential for cognitive impairment. *Journal of Psychoactive Drugs*, *35*(2), 209–18. http://doi.org/10.1080/02791072.2003.10400002

Copenhaver, M. M., & Lee, I. C. (2006). Optimizing a community-friendly HIV risk reduction intervention for injection drug users in treatment: A structural equation modeling approach. *Journal of Urban Health*, *83*(6), 1132–1142. http://doi.org/10.1007/s11524-006-9090-1

Copenhaver, M. M., Lee, I.-C., & Baldwin, P. (2013). A Randomized Controlled Trial of the Community-Friendly Health Recovery Program (CHRP) Among High-Risk Drug Users in Treatment. *AIDS and Behavior*, *17*(9), 2902–2913. http://doi.org/10.1007/s10461-013-0539-4

Copenhaver, M. M., Lee, I.-C., & Margolin, A. (2007). Successfully integrating an HIV risk reduction intervention into a community-based substance abuse treatment program. *The American Journal of Drug and Alcohol Abuse*, *33*(1), 109–20. http://doi.org/10.1080/00952990601087463

Copenhaver, M., Shrestha, R., Wickersham, J. A., Weikum, D., & Altice, F. L. (2016). An Exploratory Factor Analysis of a Brief Self-Report Scale to Detect Neurocognitive

Impairment Among Participants Enrolled in Methadone Maintenance Therapy. *Journal of Substance Abuse Treatment*, *63*, 61–5. http://doi.org/10.1016/j.jsat.2016.01.002

Corsi, K. F., Dvoryak, S., Garver-Apgar, C., Davis, J. M., Brewster, J. T., Lisovska, O., & Booth, R. E. (2014). Gender differences between predictors of HIV status among PWID in Ukraine. *Drug and Alcohol Dependence*, *138*(1), 103–108. http://doi.org/10.1016/j.drugalcdep.2014.02.012

Crepaz, N., Lyles, C. M., Wolitski, R. J., Passin, W. F., Rama, S. M., Herbst, J. H., … Stall, R. (2006). Do prevention interventions reduce HIV risk behaviours among people living with HIV? A meta-analytic review of controlled trials. *AIDS*, *20*(2), 143–157. http://doi.org/10.1097/01.aids.0000196166.48518.a0

Dore, G. J., McDonald, A., Li, Y., Kaldor, J. M., & Brew, B. J. (2003). Marked improvement in survival following AIDS dementia complex in the era of highly active antiretroviral therapy. *AIDS (London, England)*, *17*(10), 1539–1545. http://doi.org/10.1097/01.aids.0000076282.54156.c3

Ezeabogu, I., Copenhaver, M. M., & Potrepka, J. (2012). The influence of neurocognitive impairment on HIV treatment outcomes among drug-involved people living with HIV/AIDS. *AIDS Care*, *24*(3), 386–393. http://doi.org/10.1080/09540121.2011.608794

Fisher, J. D., Cornman, D. H., Osborn, C. Y., Amico, K. R., Fisher, W. A., & Friedland, G. A. (2004). Clinician-initiated HIV risk reduction intervention for HIV-positive persons: Formative Research, Acceptability, and Fidelity of the Options Project. *Journal of Acquired Immune Deficiency Syndromes (1999)*, *37 Suppl 2*, S78–87. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15385903

Gandhi, N. S., Moxley, R. T., Creighton, J., Roosa, H. V., Skolasky, R. L., Selnes, O. A., … Sacktor, N. (2010). Comparison of scales to evaluate the progression of HIV-associated neurocognitive disorder. *HIV Therapy*, *4*(3), 371–379. http://doi.org/10.2217/hiv.10.23

Gonzalez, R., Vassileva, J., Bechara, A., Grbesic, S., Sworowski, L., Novak, R. M., … Martin, E. M. (2005). The influence of executive functions, sensation seeking, and HIV serostatus on the risky sexual practices of substance-dependent individuals. *Journal of the International Neuropsychological Society : JINS*, *11*(2), 121–31. http://doi.org/10.1017/S1355617705050186

Grenard, J. L., Ames, S. L., & Stacy, A. W. (2013). Deliberative and spontaneous cognitive processes associated with HIV risk behavior. *Journal of Behavioral Medicine*, *36*(1), 95–107. http://doi.org/10.1007/s10865-012-9404-6.Deliberative

Heaton, R. K., Franklin, D. R., Ellis, R. J., McCutchan, J. A., Letendre, S. L., LeBlanc, S., … Grant, I. (2011). HIV-associated neurocognitive disorders before and during the era of combination antiretroviral therapy: Differences in rates, nature, and predictors. *Journal of NeuroVirology*, *17*(1), 3–16. http://doi.org/10.1007/s13365-010-0006-1

Huedo-Medina, T. B., Boynton, M. H., Warren, M. R., LaCroix, J. M., Carey, M. P., & Johnson, B. T. (2010). Efficacy of HIV Prevention Interventions in Latin American and

Caribbean Nations, 1995–2008: A Meta-Analysis. *AIDS and Behavior*, *14*(6), 1237–1251. http://doi.org/10.1007/s10461-010-9763-3

Huedo-Medina, T. B., Shrestha, R., & Copenhaver, M. (2016). Modeling a Theory-Based Approach to Examine the Influence of Neurocognitive Impairment on HIV Risk Reduction Behaviors Among Drug Users in Treatment. *AIDS and Behavior*. http://doi.org/10.1007/s10461-016-1394-x

Imai, K., Keele, L., Tnigley, D., & Yamamoto, T. (2010). Causal Mediation Analysis Using R ∗. In *Advances in social science research using R* (pp. 129–154). Springer New York.

Indlekofer, F., Piechatzek, M., Daamen, M., Glasmacher, C., Lieb, R., Pfister, H., … Schütz, C. G. (2009). Reduced memory and attention performance in a population-based sample of young adults with a moderate lifetime use of cannabis, ecstasy and alcohol. *Journal of Psychopharmacology (Oxford, England)*, *23*(5), 495–509. http://doi.org/10.1177/0269881108091076

Inrig, S. (2015). Book Review: The Origin of AIDS by Jaques Pepin, New York: Cambridge University Press, 2011. *Journal of Medical Humanities*, *36*(3), 257–258. http://doi.org/10.1007/s10912-014-9291-7

Kalichman, S. C. (2008). Co-occurrence of treatment nonadherence and continued HIV transmission risk behaviors: implications for positive prevention interventions. *Psychosomatic Medicine*, *70*(5), 593–7. http://doi.org/10.1097/PSY.0b013e3181773bce

Lee, Y. H., Salman, A., & Cooksey-James, T. (2016). Gender Differences in HIV / AIDS Preventive Self-efficacy among Taiwanese Adolescents. *AIDS Education and Prevention*, *28*(1), 77–89.

Li, L., Wu, Z., Liang, L. J., Lin, C., Zhang, L., Guo, S., … Li, J. (2013). An intervention targeting service providers and clients for methadone maintenance treatment in China: A cluster-randomized trial. *Addiction*, *108*(2), 356–366. http://doi.org/10.1111/j.1360-0443.2012.04020.x

Lovejoy, T. I., & Suhr, J. A. (2009). The relationship between neuropsychological functioning and HAART adherence in HIV-positive adults: a systematic review. *Journal of Behavioral Medicine*, *32*(5), 389–405. http://doi.org/10.1007/s10865-009-9212-9

Lundqvist, T. (2005). Cognitive consequences of cannabis use: Comparison with abuse of stimulants and heroin with regard to attention, memory and executive functions. *Pharmacology Biochemistry and Behavior*, *81*(2 SPEC. ISS.), 319–330. http://doi.org/10.1016/j.pbb.2005.02.017

MacKinnon, D. P. (2008). *Introduction to Statistical Mediation Analysis*. Routledge. Retrieved from https://books.google.com/books?hl=en&lr=&id=vHUVYKfrdtYC&pgis=1

MacKinnon, D. P., Fairchild, A. J., & Fritz, M. S. (2007). Mediation Analysis. *THe Annual Review of Psychology*, *58*, 593–614.

http://doi.org/10.1146/annurev.psych.58.110405.085542

Maremmani, I., Pani, P. P., Pacini, M., & Perugi, G. (2007). Substance use and quality of life over 12 months among buprenorphine maintenance-treated and methadone maintenance-treated heroin-addicted patients. *Journal of Substance Abuse Treatment*, *33*(1), 91–8. http://doi.org/10.1016/j.jsat.2006.11.009

Marshall, B. D. L., Friedman, S. R., Monteiro, J. F. G., Paczkowski, M., Tempalski, B., Pouget, E. R., … Galea, S. (2014). Prevention and treatment produced large decreases in HIV incidence in a model of people who inject drugs. *Health Affairs (Project Hope)*, *33*(3), 401–9. http://doi.org/10.1377/hlthaff.2013.0824

Mateu-Gelabert, P., Harris, S., Berbesi, D., Segura Cardona, Á. M., Montoya Vélez, L. P., Mejía Motta, I. E., … Friedman, S. R. (2016). Heroin Use and Injection Risk Behaviors in Colombia: Implications for HIV/AIDS Prevention. *Substance Use & Misuse*, *51*(2), 230–40. http://doi.org/10.3109/10826084.2015.1092989

Mathers, B. M., Degenhardt, L., Bucello, C., Lemon, J., Wiessing, L., & Hickman, M. (2013). Mortality among people who inject drugs: a systematic review and meta-analysis. *Bulletin of the World Health Organization*, *91*(2), 102–123. http://doi.org/10.2471/BLT.12.108282

Mathers, B. M., Degenhardt, L., Phillips, B., Wiessing, L., Hickman, M., Strathdee, S. A., … Mattick, R. P. (2008). Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review. *The Lancet*, *372*(9651), 1733–1745. http://doi.org/10.1016/S0140-6736(08)61311-2

Meade, C. S., Conn, N. A., Skalski, L. M., & Safren, S. A. (2011). Neurocognitive impairment and medication adherence in HIV patients with and without cocaine dependence. *Journal of Behavioral Medicine*, *34*(2), 128–138. http://doi.org/10.1007/s10865-010-9293-5

Miner, M. H., Peterson, J. L., Welles, S. L., Jacoby, S. M., & Rosser, B. R. (2009). How Do Social Norms Impact HIV Sexual Risk Behavior in HIV Positive Positive Men Who Have Sex with Men : Multiple Mediator Effects. *Journal of Health Psychology*, *14*(6), 761–770. http://doi.org/10.1177/1359105309338976.How

Mitchell, M. M., Severtson, S. G., & Latimer, W. W. (2007). Interaction of cognitive performance and knowing someone who has died from aids on HIV risk behaviors. *AIDS Education and Prevention*, *19*(4), 289–297. http://doi.org/10.1521/aeap.2007.19.4.289

Nath, a, Maragos, W. F., Avison, M. J., Schmitt, F. a, & Berger, J. R. (2001). Acceleration of HIV dementia with methamphetamine and cocaine. *Journal of Neurovirology*, *7*(1), 66–71. http://doi.org/10.1080/135502801300069737

Nehl, E. J., Klein, H., Sterk, C. E., & Elifson, K. W. (2015). Prediction of HIV Sexual Risk Behaviors Among Disadvantaged African American Adults Using a Syndemic Conceptual Framework. *AIDS and Behavior*, *20*(2), 449–460. http://doi.org/10.1007/s10461-015-1134-7

Noar, S. M. (2008). Behavioral interventions to reduce HIV-related sexual risk behavior: review and synthesis of meta-analytic evidence. *AIDS and Behavior*, *12*(3), 335–53. http://doi.org/10.1007/s10461-007-9313-9

NSDUH. (2010). Results from the 2010 National Survey on Drug Use and Health : Mental Health Findings. *Measurement*.

Otiashvili, D., Piralishvili, G., Sikharulidze, Z., Kamkamidze, G., Poole, S., & Woody, G. E. (2013). Methadone and buprenorphine-naloxone are effective in reducing illicit buprenorphine and other opioid use, and reducing HIV risk behavior--outcomes of a randomized trial. *Drug and Alcohol Dependence*, *133*(2), 376–82. http://doi.org/10.1016/j.drugalcdep.2013.06.024

Pabst, A., Kraus, L., Piontek, D., Mueller, S., & Demmel, R. (2014). Direct and indirect effects of alcohol expectancies on alcohol-related problems. *Psychology of Addictive Behaviors*, *28*(1), 20–30. http://doi.org/10.1037/a0031984

Pitpitan, E. V, Patterson, T. L., Abramovitz, D., Vera, A., Martinez, G., Staines, H., & Strathdee, S. A. (2015). Policing Behaviors, Safe Injection Self-Efficacy, and Intervening on Injection Risks: Moderated Mediation Results From a Randomized Trial. *Health Psychology*, *35*(1), No Pagination Specified. http://doi.org/10.1037/hea0000241

Puffer, E. S., Meade, C. S., Drabkin, A. S., Broverman, S. A., Ogwang-Odhiambo, R. A., & Sikkema, K. J. (2011). Individual- and family-level psychosocial correlates of HIV risk behavior among youth in rural Kenya. *AIDS and Behavior*, *15*(6), 1264–74. http://doi.org/10.1007/s10461-010-9823-8

Robertson, K. R., Smurzynski, M., Parsons, T. D., Wu, K., Bosch, R. J., Wu, J., … Ellis, R. J. (2007). The prevalence and incidence of neurocognitive impairment in the HAART era. http://doi.org/10.1097/QAD.0b013e32828e4e27

Royal, W., Cherner, M., Burdo, T. H., Umlauf, A., Letendre, S. L., Jumare, J., … Blattner, W. A. (2016). Associations between Cognition, Gender and Monocyte Activation among HIV Infected Individuals in Nigeria. *PlOS oneS One*, *11*(2), e0147182. http://doi.org/10.1371/journal.pone.0147182

Sacktor, N. C., Lyles, R. H., Skolasky, R. L., Kleeberger, C., Selnes, O., Miller, E., … JC, M. (1999). Combination antiretroviral therapy improves psychomotor speed performance in HIV-seropositive homosexual men. Multicenter AIDS Cohort Study (MACS). *Neurology*, *52*(8), 1640–1647.

Sacktor, N. C., Skolasky, R. L., Lyles, R. H., Esposito, D., Selnes, O. A., & McArthur, J. C. (2000). Improvement in HIV-associated motor slowing after antiretroviral therapy including protease inhibitors. *Journal of Neurovirology*, *6*(1), 84–88. http://doi.org/10.3109/13550280009006385

Sacktor, N., McDermott, M. P., Marder, K., Schifitto, G., Selnes, O. a, McArthur, J. C., … Epstein, L. (2002). HIV-associated cognitive impairment before and after the advent of combination therapy. *Journal of Neurovirology*, *8*(2), 136–142.

http://doi.org/10.1080/13550280290049615

Schouten, J., Cinque, P., Gisslen, M., Reiss, P., & Portegies, P. (2011). HIV-1 infection and cognitive impairment in the cART era: a review. *AIDS (London, England)*, *25*(5), 561–575. http://doi.org/10.1097/QAD.0b013e3283437f9a

Schuster, R. M., Crane, N. A., Mermelstein, R., & Gonzalez, R. (2012). The influence of inhibitory control and episodic memory on the risky sexual behavior of young adult cannabis users. *Journal of the International Neuropsychological Society : JINS*, *18*(5), 827–33. http://doi.org/10.1017/S1355617712000586

Scott-Sheldon, L. A. J., Huedo-Medina, T. B., Warren, M. R., Johnson, B. T., & Carey, M. P. (2011). Efficacy of Behavioral Interventions to Increase Condom Use and Reduce Sexually Transmitted Infections. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *58*(5), 489–498. http://doi.org/10.1097/QAI.0b013e31823554d7

Sharp, P. M., & Hahn, B. H. (2011). Origins of HIV and the AIDS pandemic. *Cold Spring Harbor Perspectives in Medicine*, *1*(1), 1–22. http://doi.org/10.1101/cshperspect.a006841

Shi, J., Zhao, L.-Y., Epstein, D. H., Zhao, C., Shuai, Y., Yan, B., … Lu, L. (2007). The effect of methadone maintenance on illicit opioid use, human immunodeficiency virus and hepatitis C virus infection, health status, employment, and criminal activity among heroin abusers during 6 months of treatment in china. *Journal of Addiction Medicine*, *1*(4), 186–90. http://doi.org/10.1097/ADM.0b013e318156cc19

Shrestha, R., & Copenhaver, M. (2016). The Influence of Neurocognitive Impairment on HIV Risk Behaviors and Intervention Outcomes among High-Risk Substance Users: A Systematic Review. *Frontiers in Public Health*, *4*, 16. http://doi.org/10.3389/fpubh.2016.00016

Shrestha, R., Huedo-Medina, T. B., & Copenhaver, M. M. (2015). Sex-Related differences in Self-Reported neurocognitive impairment among High-Risk cocaine users in methadone maintenance treatment program. *Substance Abuse: Research and Treatment*, *9*, 17–24. http://doi.org/10.4137/SART.S23332

Stacy, A. W., Newcomb, M. D., & Ames, S. L. (2000). Implicit Cognition and HIV Risk Behavior. *Journal of Behavioral Medicine*, *23*(5), 475–499. http://doi.org/10.1023/A:1005577132666

Stevens, S. J., Murphy, B. S., & McKnight, K. (2003). Traumatic stress and gender differences in relationship to substance abuse, mental health, physical health, and HIV risk behavior in a sample of adolescents enrolled in drug treatment. *Child Maltreatment*, *8*(1), 46–57. http://doi.org/10.1177/1077559502239611

Strathdee, S. A., Hallett, T. B., Bobrova, N., Rhodes, T., Booth, R., Abdool, R., & Hankins, C. A. (2010). HIV and risk environment for injecting drug users: the past, present, and future. *Lancet (London, England)*, *376*(9737), 268–84. http://doi.org/10.1016/S0140-6736(10)60743-X

Tan, J. Y., Huedo-Medina, T. B., Warren, M. R., Carey, M. P., & Johnson, B. T. (2012). A meta-analysis of the efficacy of HIV/AIDS prevention interventions in Asia, 1995–2009. *Social Science & Medicine*, *75*(4), 676–687. http://doi.org/10.1016/j.socscimed.2011.08.038

Thomas, B., Mimiaga, M. J., Menon, S., Chandrasekaran, V., Murugesan, P., Swaminathan, S., … Safren, S. A. (2009). Unseen and unheard: predictors of sexual risk behavior and HIV infection among men who have sex with men in Chennai, India. *AIDS Education and Prevention : Official Publication of the International Society for AIDS Education*, *21*(4), 372–83. http://doi.org/10.1521/aeap.2009.21.4.372

Troncoso, F. T., & Conterno, L. de O. (2015). Prevalence of neurocognitive disorders and depression in a Brazilian HIV population. *Revista Da Sociedade Brasileira de Medicina Tropical*, *48*(4), 390–398. http://doi.org/10.1590/0037-8682-0034-2015

Turner, C. F., Rogers, S. M., Hendershot, T. P., Miller, H. G., & Thornberry, J. P. (1996). Improving representation of linguistic minorities in health surveys. *Public Health Reports (Washington, D.C. : 1974)*, *111*(3), 276–9. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1381773&tool=pmcentrez&rendertype=abstract

Tyor, W. R., & Middaugh, L. D. (1999). Do alcohol and cocaine abuse alter the course of HIV-associated dementia complex? *Journal of Leukocyte Biology*, *65*(4), 475–81. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10204576

UNAIDS. (2012). Global Report: UNAIDS Report on the Global AIDS Epidemic 2012. *UNAIDS*, 96. Retrieved from papers2://publication/uuid/4467B415-2E9B-472A-89EF-B30E692EFE5C

Unaids. (2013). *GLOBAL REPORT: UNAIDS report on the global AIDS epidemic 2013*. *UNAIDS*. http://doi.org/JC2502/1/E

UNAIDS. (2014). The gap report. *UNAIDS*, 422.

Unaids, W. (2009). AIDS Epidemic Update 2009. *Joint United Nations Programme on HIVAIDS UNAIDS and World Health Organization WHO*, *10*(22.07.10), 100. http://doi.org/UNAIDS/09.36E / JC1700E

Vik, P. W., Cellucci, T., Jarchow, A., & Hedt, J. (2004). Cognitive impairment in substance abuse. *Psychiatric Clinics of North America*, *27*(1), 97–109. http://doi.org/10.1016/S0193-953X(03)00110-2

Volkow, N. D., & Montaner, J. (2011). The urgency of providing comprehensive and integrated treatment for substance abusers with HIV. *Health Affairs (Project Hope)*, *30*(8), 1411–9. http://doi.org/10.1377/hlthaff.2011.0663

Vonmoos, M., Hulka, L. M., Preller, K. H., Jenni, D., Baumgartner, M. R., Stohler, R., … Quednow, B. B. (2013). Cognitive dysfunctions in recreational and dependent cocaine users: Role of attention-deficit hyperactivity disorder, craving and early age at onset.

British Journal of Psychiatry, *203*(1), 35–43. http://doi.org/10.1192/bjp.bp.112.118091

WHO. (2000). World Health Organization Drug Injecting Study. Phase II operations manual. *WHO*, 1–98.

WHO. (2014). CONSOLIDATED GUIDELINES ON HIV PREVENTION, DIAGNOSIS, TREATMENT AND CARE FOR KEY POPULATIONS. *WHO*, 184.

Winningham, A., Corwin, S., Moore, C., Richter, D., Sargent, R., & Gore-Felton, C. (2004). The changing age of HIV: Sexual risk among older African American women living in rural communities. *Preventive Medicine*, *39*(4), 809–814. http://doi.org/10.1016/j.ypmed.2004.03.005

Woicik, P. A., Moeller, S. J., Alia-klein, N., Maloney, T., Tanya, M., Yeliosof, O., … Goldstein, R. Z. (2009). The Neuropsychology of Cocaine Addictin: Recent Cocaine Use Masks Impairment. *Neuropsychopharmacology*, *34*(5), 1112–1122. http://doi.org/10.1038/npp.2008.60.The

Worley, M., Tata, S., Granholm, E., & Brown, S. (2014). Mediated and Moderated Effects of Neurocognitive Impairment on Outcomes of Treatment for Substance Dependence and Major Depression. *Journal of Consulting and Clinical Psychology*, *82*(3), 418–428. http://doi.org/10.1530/ERC-14-0411.Persistent

Zandmomen, Z., Sardashti, S., Firouzeh, M. M., Aminabad, F. J., Ghanbariragheb, H., SeyedAlinaghi, S., & Mohraz, M. (2014). Addressing predictors of HIV related risk behaviors: Demographic and psychosocial profile of Iranian patients. *Journal of Infection and Public Health*, *7*(6), 472–480. http://doi.org/10.1016/j.jiph.2014.07.014