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Predictors and Profiles of Antiretroviral Therapy Adherence Among African-American Adolescents and Young Adult Males Behaviorally-Infected with HIV: A Classification Tree Analysis Approach

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PREDICTORS AND PROFILES OF ANTIRETROVIRAL THERAPY ADHERENCE AMONG AFRICAN-AMERICAN ADOLESCENTS AND YOUNG ADULT MALES BEHAVIORALLY-INFECTED WITH HIV: A CLASSIFICATION TREE ANALYSIS APPROACH

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
HIV	Human Immunodeficiency Virus
UNAIDS	United Nations Programme on HIV/AIDS
CDC	Center for Disease Control and Prevention
ART	Antiretroviral Therapy
USDHHS	United States Department of Health and Human Services
YAAM	Young Adult and Adolescent African-American Males
ODA	Optimal Data Analysis
CTA	Classification Tree Analysis
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NPV	Negative Predictive Value
PAC	Percentage Accuracy in Classification
ESS	Effect Strength Sensitivity

ABSTRACT

Adherence to antiretroviral therapy is crucial for thwarting disease progression and reducing secondary transmission, yet HIV+ youth struggle with adherence. The highest rates of new HIV infections occur in young African American men (YAAM), thus understanding reasons for non-adherence in this group is critical. Reasons for non-adherence can be complex and multifactorial, and innovative methods of exploration are needed for advancing prevention and treatment efforts. A sample of 387 HIV+ YAAM who reported currently taking HIV medications were selected from a cross-sectional assessment of 2,226 HIV+ youth from sites within the Adolescent Trials Network for HIV/AIDS Interventions (ATN) from 2010-2012 (12-24 years-old, *Median* = 22.00, *SD* 2.08). Participants completed self-reported adherence, demographic, health, and psychosocial measures. Seventy-two theoretically relevant predictors of adherence underwent Optimal Data Analysis (ODA) to construct a classification tree which hierarchically maximizes the classification accuracy of 100% adherence. Sixty-two percent reported 100% adherence (no missing doses) over the past seven days. Frequency of cannabis use was the strongest predictor of adherence, yielding moderate effect strength sensitivity, $ESS = 27.1$, $p < 0.00$. Among participants with infrequent cannabis use, 72% demonstrated full adherence, while only 45% of participants who used cannabis (monthly or more) demonstrated full adherence. Classification tree analysis (CTA) correctly classified 82.35% of those who were adherent and 64.85% of those who were

non-adherent. The final CTA adherence model was moderate in effect size strength (*ESS* = 38.00) identifying two pathways towards adherence and three pathways toward non-adherence. Participants most likely to be adherent were those with low levels of psychiatric distress and infrequent alcohol use (82.17% were adherent). This research demonstrates the impact of substance use and mental health on adherence among YAAM. Moreover, this analysis identifies complex and multiple profiles of adherence among HIV+ YAAM and suggests that targeted interventions may be most prudent. The implications of these findings and how they can serve as a guide to future research and intervention are discussed.

CHAPTER ONE

INTRODUCTION

HIV Overview

Acquired Immunodeficiency Syndrome (AIDS) is a global epidemic that has taken the lives of millions of individuals over the last 30 years. Human Immunodeficiency Virus (HIV) is the specific virus that causes AIDS (Karim, Karim, & Detels, 2008; Weiss, 1993). HIV is a retrovirus, which engenders immune system deficiency in an infected person, and AIDS is conceptualized as the "end stage" of the HIV disease (Weiss, 1993). Retroviruses are a highly complex class of virus that are able to cunningly invade body cells and infuse their DNA with the host cell DNA (Maertens, Hare, & Cherepanov, 2010). When someone is infected with HIV, the HIV viral particles seek out and bind to important types of white blood cells (e.g., CD 4+ T cells). HIV viremia (virus particles) destroy these white blood cells, which are instrumental in coordinating the host body's immunological functioning. Normally, a healthy immune system is able to jettison foreign virus particles, however in the case of retroviruses, even if the host body is able to exorcise virus viremia, the virus remains infused into the cell DNA and will be reproduced again (Neufeldt, 2010). Thus, HIV viremia is present in a host body indefinitely. And although HIV is a type of slow growing disease (i.e., the median progression to AIDS after initial infection in the United States (US) is 9-10 years; Lemp et al., 1990; Pantaleo, Graziosi, & Fauci, 1993; Hessol et al., 1994), an untreated

person living with HIV, will eventually develop AIDS, and will most likely die as a result of developing an opportunistic infection related to AIDS (e.g., Pneumocystis pneumonia; Pantaleo et al., 1993).

There are two forms of HIV; HIV-1 and HIV-2 (Hunt, 2000; Karim et al., 2008). HIV-2 is less viral than HIV-1 and is mostly limited to West Africa. For the purpose of this project all references to HIV/AIDS are referring to HIV-1. Worldwide HIV infection continues to be growing rapidly, especially in developing countries with limited access to treatment. In 2012 alone, over 1.6 million individuals lost their lives to AIDS worldwide and another 35.3 million individuals were identified as living with either AIDS or HIV (The Joint United Nations Programme on HIV/AIDS [UNAIDS], 2013). The disease is spread rapidly through a number of transmission routes (as explicated below) and over 25% of the current worldwide population infected with the disease is under the age of 25 years. Although the HIV prevalence rate is relatively low (below 1%) in the US, it has had a drastic impact on specific communities, such as disadvantaged minority populations and the gay community (Center for Disease Control and Prevention [CDC], 2011; Hall, Byers, Ling, & Espinoza, 2007; Nelson, 2002; Sutton, et al., 2009) as well as entire geographic areas (i.e., Southeastern US).

Currently, there is no cure for HIV/AIDS, however, significant pharmacological advances in the treatment of HIV have been developed, which has greatly extended the life expectancy of individuals diagnosed with the disease (Fang et al., 2007; Palmisano, & Vella, 2011; The Antiretroviral Therapy Cohort Collaboration, 2008). Since 1996, Antiretroviral Therapy (ART) has been the standard of care for limiting HIV disease

progression and the development of AIDS (Dybul et al., 2002; The Antiretroviral Therapy Cohort Collaboration, 2008). Highly Active ART is the combination of three or more antiretroviral medications (ARVs) that when taken together have stronger efficacy for reducing the deleterious effects of HIV/AIDS. Moreover, when individuals take a combination of ARVs they are less likely to become resistant to any one of the specific ARVs than if they were only taking one ARV at a time (Palmisano, & Vella, 2011). Research has shown that ART is particularly effective for reducing the number of HIV viral particles in the bloodstream (Montaner et al., 1998) and increasing the number of CD4+ T cells (which coordinates the body's immunological functioning; Paterson et al., 2000). However, in order for ART to be effective in treating HIV disease progression, a greater than 95% adherence rate is required (Paterson et al., 2000; Low-Beer, Yip, O'Shaughnessy, Hogg, & Montaner, 2000). If this high level of medication adherence is not achieved by an individual infected with HIV, the likelihood of achieving an undetectable viral load is dramatically reduced. As a result the individual's immune system will not be able to suppress the production of HIV viremia and their CD4+ T cell count will decrease, allowing opportunistic infections that are associated with AIDS (e.g., Kaposi Sarcoma) to infect the body and eventually lead to the individual's death (Paterson et al., 2000). In addition, sub-adherent individuals are also at risk for becoming resistant to ART (Low-Beer et al., 2000). Recent research, however, suggests that the need for near perfect adherence rates, may vary depending on the class of medication being prescribed, as well as the frequency of the dose (i.e., those taking once a day pills may have significant viral reloading even after just missing one pill; Caims, 2010;

Maggiolo et al., 2007). That being said, the current standard of HIV care strongly recommends strict adherence to ART for optimal health outcomes (United States Department of Health and Human Services [US DHHS]).

In the US, research indicates that African-Americans (Bogart, Wagner, Galvan, & Klein, 2010) and adolescents (Chesney, Ickovics, Chamber, & Gifford, 2000; Murphy et al., 2001) are demographic groups that are at the greatest risk for initial HIV infection. In addition, both of these groups have consistently evidenced sub-optimal ART adherence rates (Bogart et al., 2010; Murphy et al., 2003; Rao, Kekwaletswe, Hosek, Martinez, & Rodriguez, 2007). African-American males who are behaviorally-infected with HIV, comprise the greatest percentage of all individuals infected with HIV and have ART adherence rates that are worse than their Caucasian or Latino counterparts (Hall et al., 2007). The term "behaviorally-infected" refers to individuals who contracted the disease as a result of their own behavior, as opposed to being perinatally infected. According to the CDC in 2011, males, between the ages of 13-29, from racial and ethnic minority groups are the fastest growing group of newly-HIV-infected individuals in the US. Moreover, as mentioned above, these individuals demonstrate extremely poor ART adherence rates. Non-adherence to ART regimens is problematic, as poor adherence to ART protocols among individuals living with HIV/AIDS has been consistently associated with high HIV viral load, increase risk for opportunistic infection, and higher rates of mortality (Kahana, Rohan, Allison, Frazier, & Drotar, 2012; Paterson et al., 2000). Furthermore, poor adherence to ART is a significant public health concern for the following reasons: (a) ART adherence is the greatest predictor of decreased HIV/AIDS

progression (Paterson et al., 2000); (b) inconsistent ART adherence significantly reduces the effectiveness of ARVs in the future (Chesney, Ickovics, Chamber, & Gifford, 2000), as the body builds immunity to the medication; and (c) individuals with inconsistent ART adherence are at greater risk for transmitting HIV to others and transmitting mutated ARV resistant strains of HIV than individuals who are fully adherent with ART (Low-Beer et al., 2000).

Although young adult and adolescent African-American males (YAAM) represent a demographic group that is both at great risk for HIV infection and once infected with this disease, ART non-adherence, there is a dearth of research investigating the barriers and predictors of ART adherence within this demographic group (Martinez et al., 2000; Rao et al., 2007). The few studies that do exist, do not thoroughly examine the complex relationships of factors, which may influence ART adherence behavior among this "high-risk" demographic group. Thus, we currently lack an elucidated understanding of how mechanisms of risk or protection that pertain to YAAM behaviorally-infected with HIV interact to impact ART adherence outcomes. Therefore, further research is required to understand how variables which have been indicated to be related to adherence outcomes among YAAM males (i.e., depressive symptoms, substance abuse, age, HIV stigma, self-efficacy, and social support) interact to influence ART adherence. Furthermore, with regard to this demographic group, it is essential to identify contexts of increased risk for ART non-adherence, contexts which buffer against non-adherence, and to illustrate what the specific profiles or pathways of adherence are for these youth. Lastly, a more complete understanding of the attributes that increase or buffer risk may have the

potential to attenuate non-adherence behaviors among this high-risk group, as more effective intervention and prevention programs can be created to target the most notable risk and protective factors.

Therefore, the primary aim of this study is to identify the strongest predictors and profiles (i.e., the specific pathways) of ART adherence and non-adherence among YAAM who have been behaviorally-infected with HIV. Specifically, this study identifies the strongest attribute (among a myriad of theoretically-driven predictors) that has the greatest predictive strength for correctly classifying ART adherence outcomes among a high-risk group for ART non-adherence, from a large, multisite sample. Secondly, this study constructs a nonlinear multi-attribute tree model of ART adherence that illuminates the profiles of adherence for YAAM who have been behaviorally-infected with HIV. Finally, this study allows for an understanding of how commonly cited predictors of adherence (e.g., psychiatric illness, self-efficacy, etc) interact and identifies important moderators of increased protection or risk related to ART adherence behaviors within this group.

In order to create a predictive model of ART adherence which maximizes the classification accuracy of adherence outcomes, this study employed the use of an innovative statistical technique known as Optimal Data Analysis (ODA). ODA is a statistical analysis that maximizes classification accuracy of a dichotomous outcome (i.e., adherence vs. non-adherence; Suzuki, Bryant, Edwards, 2010; Yarnold & Stolystik, 2005). Unlike statistical techniques that maximize a variance ratio (i.e., the average effect of independent variables on outcomes across all study participants), ODA classifies the

sample with optimal accuracy, as likely to fall into one of two categories of the dependent variable (e.g., being ART adherent or non-adherent). ODA is a nonparametric analysis and therefore does not have to meet the assumptions of parametric tests (e.g., normality of distribution, independence, and linearity). ODA uses an exact permutation probability and produces an always valid Type-1 error rate (Yarnold & Soltysik, 2005).

In addition, ODA allows for the creation of a classification tree analysis (CTA) model; a nonlinear multi-attribute tree model, which hierarchically maximizes the mean percent accuracy classification of a dichotomous outcome (e.g., adherence or non-adherence). The final CTA model construction will include the combination of successive predictors that most accurately predict ART adherent or non-adherent behaviors. The assumption that the attributes are important for all members of a sample does not exist. Instead, ODA is used to identify which predictors are most sensitive for maximizing classification accuracy for distinct subsets of a sample (Smith et al., 2010). Lastly, the same attribute may appear more than once in a model (based on the classification of different subsamples in the model) and both the direction and coefficient of an attribute may also vary for different subsamples of the overall sample (Yarnold & Soltysik, 2005).

The current study extends and make important contributions to the ART adherence literature in several notable ways: (a) The population selected for study (African-American adolescent and young adult males behaviorally-infected with HIV) although at great risk for HIV infection and subsequently after infection ART non-adherence, has been understudied with regard to the factors that influence ART adherence; (b) To my knowledge this is the first study to apply ODA to identify the

strongest predictors and pathways of ART adherence among this population; (c) This study identifies contexts of increased risk, as well as protective factors that may buffer against non-adherence, and the combination of factors that beget the greatest risk for ART non-adherence; (d) Results from this project can be used to inform ART adherence intervention and prevention programs; (e) Primary medical providers will be able to use the findings from this study to identify the patients at greatest risk for ART non-adherence and modify treatment approaches appropriately.

CHAPTER TWO

BACKGROUND AND SIGNIFICANCE

History of HIV in the United States

In the United States the first cases of HIV/AIDS were reported in 1981, when groups of gay men in Los Angeles, New York City, and San Francisco began developing Kaposi Sarcoma, an extremely rare tumor among the general population and pneumocystis carinii pneumonia (fungal infection of the lungs) without identifiable etiology (CDC, 2006; Karim, et al., 2008). During the 1980's the incident rate of HIV/AIDS exploded, climaxing in 1992 with roughly 78,000 new cases (across all demographic groups) diagnosed during that year (CDC, 2006). In 1998, the rate of new HIV cases began to stabilize and currently there is an estimated 56,000 new annual cases of HIV diagnosed in the United States across all demographic groups (Prejean et al., 2011). At the present time, over one million individuals in the US are living with HIV/AIDS and since the US epidemic began in 1981, over 600,000 individuals have lost their lives to the disease (CDC, 2009). However, given the significant advances in the treatment of HIV/AIDS over the past 25 years, the incidence rate of AIDS since 1992 has been reduced by as much as 40%, and individuals infected with HIV are able to live longer, healthier lives with proper treatment (CDC, 2004). For instance, as part of a multinational cohort study, The Antiretroviral Therapy Cohort Collaboration (2008), of high-income countries reported a steady increase in life expectancy among individuals

living with HIV receiving ART treatment. For example, a 20 year-old individual living with HIV at the time of ART initiation during the years of 1996-99 was estimated to live an additional 36.1 years; compared to a greater likelihood of longevity when ART initiation began during 2000-02 (41.2 years) and during 2003-05 (49.4 years). However, additional years of life expectancy among all participants and across time periods were found to be moderated by gender (42.8 years for males, 44.2 years for females), injection drug use (32.6 years for injecting drug users vs. 44.7 years for non-injecting drug users), and initial CD4+ T cell count (50.4 years for those with ≥ 200 cells m/l of blood compared to only 42.0 years for those with 100- 199 cells m/l and 32.4 years for those with < 100 cells m/l). Even among individuals in the US reaching the advanced stage of HIV (i.e.., an AIDS diagnosis) have experienced significant delays of disease advancement resulting in death. The chances of an individual living an additional two years after an AIDS diagnosis was only 44% between the years of 1981-1992 and has since progressively increased with the development of ART (e.g., 64% between the years of 1993-1995 & 85% between the years of 1996-2000; CDC, 2006).

Although, the advancement in ART treatment dramatically increases the lifespan for individuals living with HIV/AIDS, these individuals still face a significant decrease in life expectancy when compared to healthy controls. For example, The Antiretroviral Therapy Cohort Collaboration (2008) estimated that among their sample of 43,355 patients living with HIV, their life expectancy would be approximately two-thirds of the general population from their respective countries. This may be a result of the significant inflammation and organ tissue damage that results from the virus even when it is well

managed (Palmisano & Vella, 2011). Such organ tissue damage can result in greater likelihood of bone disease, cardiovascular disease, cancer, and neurocognitive declines compared to healthy controls (Marin et al., 2009). Alternatively, as postulated by The Antiretroviral Therapy Cohort Collaboration (2008), this shorter life-expectancy may be a result of other lifestyle and socioeconomic factors associated with HIV/AIDS (i.e., conditions of poverty and a lack of access to proper health care).

HIV Transmission

The explosion of HIV and AIDS in the 1980's led to comprehensive investigations of how such a virus is spread among individuals. The transmission of HIV has been found to spread through unprotected sexual intercourse (either vaginal or anal), unprotected oral sex, and sharing of needles or syringes with someone who is HIV positive. In addition, HIV can be spread from mother to infant perinatally, as well as through breast-feeding. However, great steps have been taken to reduce the mother-infant transmission of HIV and perinatal HIV infections are becoming rarer (Coutsoudis et al., 2004). Lastly, HIV infection can be transmitted through blood transfusions with infected blood; however, due to advances in blood screening, the probability of receiving an HIV infection today from a blood transfusion is less than 0.001% in the United States (APA, 2000). Based on data from 2007-2008, the likelihood of acquiring HIV infection in the US via a blood transfusion was estimated to be one in 1.5 million (Zhou et al., 2010). Since 2002 only one case of HIV infection via blood transfusion has been identified (CDC, 2010). In the US, sexual transmission accounts for approximately 86% of all HIV

infections, with syringe drug use (6%), perinatal transmission (5%), and unsafe health care practice (4%) accounting for the remaining HIV infection cases.

Transmission through sexual intercourse. The actual risk of HIV infection through a single sexual act is quite low. In a five-year longitudinal study of 174 monogamous heterosexual HIV discordant couples in Rakai, Uganda, the overall probability of HIV transmission to the uninfected partner was 0.0011 per coital act (Gray et al., 2001). This rate of HIV transmission for a single sexual act in Uganda is consistent with estimates from Europe and North America (Gray et al., 2001). Nevertheless, several factors can greatly increase the chance of HIV transmission through sexual intercourse, such as the presence of co-occurring sexually transmitted infections (STIs; especially when accompanied with genital ulcers), an uncircumcised male, intercourse during menstruation or pregnancy, receptive anal sex, and higher levels of HIV viral load among the infected individual (Attia, Egger, Muller, Zwahlen, & Low, 2009; Karim et al., 2008; Royce, Sena, Cates, & Cohen, 1997). Gray and colleagues (2001), found both HIV viral loads and genital ulcers to significantly increase the chance of HIV transmission among HIV discordant heterosexual couples during a single coital act. For example, the likelihood of HIV transmission from a single coital act increased from 0.0001 when HIV viral loads were below 1700 copies/mL to 0.0023 when viral loads were greater than 38,500 copies/mL. In addition, the rate of transmission increased among participants from 0.0011 without a genital ulcer to 0.0041 with a genital ulcer.

Consistent condom use (either male or female condoms) is an effective contraception for reducing HIV transmission rates among serodiscordant couples (Karim

et al., 2008; Royce et al., 1997). Moreover, ART has been found to significantly reduce the likelihood of HIV transmission to uninfected individuals. In Taiwan the rate of HIV transmission among citizens decreased by 53% after polices were created in 1997 to promote free access to highly active ART (Fang et al., 2004). In the United States, Porco and colleagues (2004) reported a similar decrease in HIV transmission (e.g., a 60% reduction) after the initiation of ART in a six-year longitudinal study among a sample of 534 gay males in San Francisco. Moreover, this reduction in community HIV infectivity occurred in the context of increased unprotected anal sex among participants. The first randomized clinical trial (across nine countries) to evaluate the effectiveness of ART in preventing the transmission of HIV through sexual intercourse between serodiscordant couples found a 96% reduction in HIV transmission among 1,763 HIV serodiscordant couples (Cohen, McCauley, & Gamble, 2012). Moreover, the only transmission event that occurred (in the serodiscordant couple group receiving ART) was found to take place before HIV viral levels were suppressed to undetectable levels. Hence, adherence to ART is not only the strongest treatment intervention for individuals infected with HIV, but is one of the best prevention tools for HIV infection for individuals and communities.

Transmission through blood. As mentioned above, the transmission of HIV via blood transfusions or as part of health care practices have become extremely rare in the US (Karim et al., 2008). National screening procedures for donated blood and safety precautions in hospital settings, such as single use syringes, use of disposable gloves, and biohazard waste containers have drastically reduced the likelihood of HIV infection through blood contact in a hospital setting to nearly non-existent. However, infection

through syringe sharing by illicit drug users remains problematic in counties outside of the US (e.g., Asia, Russia; Karim et al., 2008).

Perinatal transmission. The rate of HIV transmission from mother-to-child (without intervention) can vary between 20% and 40% and is affected by several key factors. Mother-to-child-transmission (MTCT) can occur in-utero (during delivery), as well as postnatally (i.e., through breast feeding). Approximately half -to –two-thirds of perinatal infections ensue in-utero with the remaining infections occurring during breast feeding (Karim et al., 2008). As with HIV transmission through sexual intercourse, higher levels of HIV viral load in the mother increases the likelihood of successful transmission of the virus. Several factors such as caesarian delivery, ARV use (for mother and infant), exclusive breast feeding or formula (not mixed feeding), and a shorter duration of breast feeding can dramatically reduce MTCT rates (Coutsoudis et al., 2004; Karim et al., 2008). Moreover, the successful combination of these factors can reduce MTCT rates to less than 1% and in the United States MTCT has been practically eliminated (Karim et al., 2008).

The Path from HIV to AIDS

After HIV is successfully transmitted from one person to another, there is a specific pathway that occurs from initial HIV infection until an AIDS diagnosis (for the majority of individuals infected with the virus). When HIV is left untreated, it results in the gradual deterioration of the body's immunological functioning. Specifically, the HIV virus enters a host cell and surreptitiously snips open the host cell's DNA and binds its own genes to the cell's DNA. A healthy immune system can jettison the initial

production of foreign viral particles; however, the production never ceases to desist, as the virus is now intertwined into the body's DNA. HIV damages the body's immune system by seeking out, infecting, and destroying vital lymphocytes (a group of white blood cells) called CD4 + T cells (also known as "T-helper cells"), as well as other cell types, such as macrophages and monocytes that enable the body to fight off infectious diseases (CDC, 2006; Pantaleo, et al., 1993; Richman, 2000). The loss of CD4+ T cells is very problematic, as these cells play a key role in coordinating an individual's immunological functioning (Fauci, 1993). These cells can be conceptualized as the "quarterbacks" of the immune system, and without the leadership of the CD4 + T cells, other white blood cells are unable to properly fight off infection.

An individual who is healthy and uninfected with HIV, is estimated to have between 800 and 1,200 CD4+ T cells per cubic millimeter (mm^3) of blood. Individuals living with HIV can experience a remarkable decline in their number of CD4+ T cells, which consequently compromises an individual's ability to fight off infection (APA, 2000). When an individual's CD4+ T cell count falls below 200/mm^3 of blood, they become susceptible to opportunistic infections that can quickly become fatal (Palacio, Kahn, Richards, & Morin, 2002). According to the CDC the current definition of AIDS (revised in 1993) is as follows: HIV progresses into the clinical condition of AIDS when a person infected with HIV, 13 years or older, has a CD4+ T cell count of less than 200/mm^3 of blood or a CD4+ T cell percentage of total lymphocytes of less than 14. At that point the individual is extremely vulnerable to opportunistic infections that can result in clinical conditions rarely seen without HIV infection, as well as suffering from

neurological conditions, other cancers, and infections of the lungs and intestinal tracts (CDC, 1992; CDC, 1999).

HIV Pathogenesis

Initial infection (acute phase). Within the first three to six weeks after initial HIV infection, HIV rapidly infects selective cell types (CD4+ T cells, macrophages, monocytes), as well as lymphoid tissue, creating a propagation of HIV viremia throughout the body (Tindall & Cooper, 1991). This results in a massive battle between HIV viremia and CD4+ T cells (APA, 2000). What transpires for the majority of individuals infected with HIV, is an initial substantial drop of CD4+ T cells and the replication of billions of HIV viremia in the bloodstream (Clark et al., 1991; Cooper et al., 1985; Daar, Moudgil, Meyer, & Ho, 1991; Pantaleo et al., 1993; Tindall, & Cooper, 1991). The decrease in CD4+ T cells is a direct result of HIV mediated cell killings, as they seek out these cell types and infect them (Fauci, 1993). During this time period, most newly-infected individuals experience mononucleosis symptoms (i.e., fever, sore throat, and fatigue). In addition, the ensuing course of the disease is affected by how successful the virus has been in planting itself in lymphoid tissue (Pantaleo et al., 1993; see figure entitled "HIV Disease Progression from Infection to Death").

Clinical latency (asymptomatic phase). Within four months of the initial HIV infection, a person's immune system responds, led by T lymphocytes and Cytotoxic B cells (CD4+ T and CD8+ cells) that seek out and destroy the more than 10 billion HIV viral particles produced in a day (Clark et al., 1991; Daar et al., 1991; Pantaleo et al., 1993). Eventually a viral "set-point" is established that represents a balance between HIV

viremia replication and the ability of the body to produce new CD4+ T cells (APA, 2000; Fauci, 1993; Pantaleo et al., 1993). After the surge of the person's immune system, there is a rapid reduction in the number of HIV viral particles and the number of CD4+ T cells increase to levels slightly below normal functioning. This period of the disease is referred to as the *clinical latency period* and can last for many years (Pantaleo et al., 1993).

Although this phase is referred to as a "latent" period, HIV viral particles still exist and lie in resting memory cells, the lymph nodes, nervous tissue, and other areas of the central nervous system (Hunt, 2000). In fact, what is occurring is a slow but steady depletion of CD4 + T cells and an eventual deterioration of one's immune system (Pantaleo et al., 1995). The progression to the symptomatic phase (the next phase in the disease) is best predicted by the persons' immune functioning prior to HIV infection and the initial viral load of the disease (APA, 2000; Tindall & Cooper, 1991). Therefore, a person's health status before being infected with HIV is an important predictor of their HIV/AIDS course. The period of clinical latency can vary from one year to over fifteen years (Hunt, 2000). In the United States, the median time between initial infection and the symptomatic phase is roughly 10 years (Lemp et al., 1990; Pantaleo et al., 1993; Hessol et al., 1994).

Symptomatic phase. Eventually the immune system is no longer able to maintain a healthy "set-point" between HIV viral replication and new CD4+ T cell production (Hunt, 2000). This is the result of CD4 + T cell dysfunction and the seeding of the disease that occurred during the initial infection period (Pantaleo, 1993). Paradoxically, the same white blood cells that destroy the HIV viremia also attack and destroy the CD4+

T cells, which have become infected with HIV. With a significant loss of CD4+ T cells and a loss of functionality for remaining CD4+ T cells, the necessary immunologic coordination to fight off infection is significantly compromised. When the level of CD4+ T cells falls below 200/mm^3 per blood, HIV viremia replication explodes and immune functioning plummets abruptly. As a result, normally benign opportunistic parasites attack the body; placing an individual at great risk for developing AIDS defining clinical conditions that are often extremely rare in the general population. After an individual is clinically diagnosed with AIDS (CD4+T cells below 200/mm3) prognosis is extremely poor, with most individuals passing away within two years without intervention (World Health Organization [WHO], 2007). The survival prospect after an AIDS diagnosis without treatment is bleak. After reviewing survival analysis studies conducted in the United States, Osmond, Charlebois, Lang, Shiboski, and Moss (1994) suggested survival rates after an AIDS diagnosis to be approximately 14 months to two years. However, length of survival after an AIDS diagnosis may in fact be shorter. For example, Bacchetti and colleagues (1989) reported a median survival rate of just 11 months among the first 500 individuals diagnosed with AIDS in San Francisco. Furthermore, a 2001 large scale study of rural Ugandans found the median survival time after an AIDS diagnosis to be just 9.2 months. Thus, although the progression from initial HIV infection to eventual death is of considerable time (9-10 years), the length of time to death is considerably short after the development of AIDS.

The HIV disease progression outlined above is typical for most individuals infected with the virus; however, there is significant variability with regard to HIV

disease progression among individuals living with this virus (Clark et al., 1991; Pantaleo, 1993; Tindall & Cooper, 1991). According to Pantaleo and colleagues (1995) a small proportion of individuals who are newly infected with HIV either show no symptoms of the disease (i.e., relatively normal CD4+ T cell count) or develop AIDS within months after initial infection and die shortly thereafter. The strongest predictor of disease progression is the level of initial HIV viral load in the bloodstream. Individuals with higher numbers of initial HIV viral load typically have a worse disease outcome (i.e., a faster development of AIDS; Hunt, 2000).

Young African-American MSM and Risk for HIV Infection

In the United States, the HIV/AIDS pandemic has disproportionally affected racial and ethnic minority groups, adolescent and young adults, and MSM at higher rates than other demographic groups (APA, 2000; CDC, 2006; Hall et al., 2007; Laurencin, Christensen, & Taylor, 2008; Palacio et al., 2002; Sutton et al., 2009). African Americans face the most severe burden of HIV of all racial/ethnic groups in the United States. Despite representing only 14% of the US population in 2009, African Americans accounted for 44% of all new HIV infections in that year (CDC, 2011). As a racial group, African-Americans are seven times more likely to be diagnosed with HIV than their Caucasian counterparts (Prejean et al., 2011). Furthermore, the rate of undiagnosed HIV infection is greater among African-Americans than Caucasians, thus skewing the true disproportion of HIV infection between demographic groups (Sutton et al., 2009).

Young people's risk for HIV infection in the US is much higher when compared to their percentage of the overall population. The term young people is defined as

individuals between the ages of 13-24 years, as described in the CDC's (2008) report on the status of HIV among youth in the US. It is currently estimated that over a quarter of all newly HIV infected individuals will be less than 24 years-old, while this age bracket comprises only 15.4% of the overall population reported in 2009 (US DHHS, 2012). The high rate of HIV infection is so prominent among young people that the age group of 20-24 years-old currently represents the age range with the highest total number of newly-infected individuals among any age bracket (CDC, 2011). In addition, young people from low-income minority backgrounds are disproportionately infected with HIV at a higher rate than Caucasian youth (Hall et al., 2007). Among all young people infected with HIV, African-Americans accounted for 65% of reported HIV infections in 2009 (CDC, 2011), an increase from a reported 55% in 2004 (CDC, 2008). This increase is even more alarming given the context that the overall rate of HIV infection for African Americans has slightly decreased (CDC, 2006). Unfortunately, although, the CDC has created programs to increase HIV awareness for youth, the rate of HIV infection in the United States for this age group within African-Americans has risen substantially (CDC, 2011).

The group of individuals with the highest rate of new HIV infections (as a percentage of their population) in the US is African-American males. In particular, the risk for HIV infection is most prominent among African-American MSM (Valleroy et al., 2001). From the years 2006-2009, of all new HIV infections among African-Americans 70% were males (CDC, 2011), and 73% of all African-American males infected with HIV were MSM. Furthermore, there has been an increased rate of HIV infection among younger MSM. Between the years of 2001-2004 there was a 14.1% increase in HIV

diagnoses among 13-19 year-olds and a 13.3% increase among 20-24 year-old MSM (Hall et al., 2007). These trends have unfortunately continued. Prejean and colleagues (2011) from the HIV Incidence Surveillance group reported a 21% increase in the HIV incidence rate among 13-29 year-olds, which was fueled by a 34% increase of HIV infection in MSM. The rise of HIV infection among MSM has mostly been the result of higher HIV infectivity rates among young African-American MSM. For example, HIV infection within young African-American MSM (13-29 years-old) has increased by an astonishing 48% between the years of 2006 and 2009 (Prejean et al., 2011). This is most alarming, given that in 2004 African-American MSM were already 19 times more likely to be diagnosed with HIV than Caucasian MSM (Hall et al., 2007).

The natural questions that arise are "why African-Americans are significantly more likely to be afflicted by this disease than other racial groups?" And "why are young African-American MSM at such high risk for acquiring HIV infection?" A common stereotype is that African-Americans are more likely to engage in high-risk behaviors (e.g., unprotected sexual intercourse, multiple partners, intravenous drug use, and fornication with sex workers) than other racial groups, which would theoretically increase the HIV infectivity rate for African-Americans. However, the empirical data generally does not support the notion that African-Americans are more likely to engage in these risky behaviors than other racial groups (CDC, 2012; Millett, Flores, Peterson, & Bakerman, 2007; Millett, Peterson, Wolitski, & Stall, 2005). In fact, Millett and colleagues (2007) conducted a meta-analysis of all published articles related to HIV and MSM between 1980 and 2006, with the purpose of explaining the HIV infectivity rate

disparity between racial/ethnic groups among MSM. This investigation yielded 53 quantitative studies and concluded that behavioral risk factors do not explain the large disparity of HIV infectivity rates between races among MSM. Research has rather identified a number of complex and intertwined social, cultural, and economic factors, such as conditions of poverty, lack of access to health care, a history of racism, and incarceration, as directly or indirectly related to the increase rate of HIV infection among African-Americans (CDC, 2008; Raymond, & McFarland, 2009).

The following amalgamation of factors reflects an empirically supported understanding of the disproportionately high rate of HIV infection among African-Americans. Early in the HIV/AIDS pandemic, studies documented a high rate of unprotected anal intercourse among African-American MSM (Heckman, Kelley, Bogart, Kalichman, & Rompa, 1999; Peterson et al., 1992), which led to a vast number of HIV infected individuals. Furthermore, there was a lack of HIV detection and proper treatment among the African-American population due to factors, such as African Americans being more likely to live in poverty and having poor access to health care (e.g., absence of health care and transportation difficulty). Subsequently, these factors have likely led to a higher background prevalence of HIV/AIDS in the African-American community than in other racial groups (Millett et al., 2007). Moreover, recent research has identified the important contribution of sexual partner selection and sexual networks to the maintenance (and even an increase among MSM) of HIV infection in African-American communities. For example, in a sample of 1,142 MSM from San Francisco, Raymond and McFarland (2009) found a three-fold likelihood (over chance) that African-American

MSM would have sexual relations with another African-American MSM. These researchers documented the potential reasons for such sexual segregation. Most notable, were the fact that African-American MSM were found to be (a) the least desired sexual partner among racial groups; (b) perceived to be a higher risk for HIV; (c) perceived to be less welcomed at San Francisco socializing venues catering to MSM; and (d) were ranked the "least easiest" to meet among all MSM. Hence, African-American MSM are more likely to be sexually restricted to within their own racial group than other MSM. Thus, since HIV is more likely to spread rapidly in highly interconnected groups (Raymond, & McFarland, 2009), African-American MSM are placed at a higher risk for HIV infection.

In addition, a meta-analysis by Millett and colleagues (2007) found that STIs play a significant role in the higher rate of HIV infection among African-Americans. Specifically, research shows that African-Americans are more likely to suffer from genital herpes, gonorrhea, chlamydia, and syphilis than their Caucasian counterparts (CDC, 2007; Millett et al., 2007; Sutton et al., 2011), all of which facilitate the transmission of HIV and places an individual at greater risk for spreading or contracting HIV during sexual interactions. This is especially true when these conditions result in genital ulcers (Fleming & Wasserheit, 1999). Furthermore, the lack of access to health care in low-income African American communities impedes the strong recommendations made by the medical community to treat STIs early, as part of comprehensive HIV prevention community programs (Nelson, 2002).

Low-income African-American communities have traditionally believed HIV transmission is the result of gay activity, a practice that is demonized by the majority of

religious leaders in these communities (Kennamer, Honnold, Bradford, & Hendricks, 2000). Young African American MSM often do not reveal their sexual preferences to family members or medical providers (Rao, et al., 2007) and are less likely to refer to themselves as gay. Rather, these individuals may refer to themselves as being "on the down low," in reference to their sexual preference of being with other men (Martinez & Hosek, 2005). Thus, individuals can be quite hesitant to inquire about their HIV seroconversion status, given the significant amount of stigma and discrimination associated with HIV in their community. As a result, HIV positive young African-American MSM are at risk to unknowingly transmit the disease until their health status deteriorates to the point where they are forced to seek out medical treatment. As explicated earlier, the process of profound immunosuppression typically occurs nine to ten years after initial infection, providing ample time for unaware HIV positive individuals to spread the disease. Although Millett and colleagues (2007) reported no differences in "ever" being tested for HIV among racial groups, they did, however, report a lower *frequency* of HIV status testing among African-American MSM. This may contribute to the increased rate of HIV infection among African-Americans by providing a longer window of transmission opportunity, as previously stated, and is reflected in the fact that HIV infected African-Americans are more likely to be identified at later stages of the disease than Caucasians (Hall et al., 2007).

Some have postulated that genetics may place African-Americans at a greater susceptibility for HIV infection than Caucasians. Research has indicated that approximately 10-11% of individuals from European descent have a genetic mutation

(known as the CCR5 receptor mutation) that creates a full or partial immunity to HIV infection compared to only 1.7% of individuals from African descent (Royce et al., 1997). However, this genetic vulnerability likely explains a minute part of the disproportionately high rate of HIV infection among African-Americans and cannot discredit the influence of the previously discussed socio-cultural factors (Laurencin et al., 2008; Millett et al., 2005; Nelson, 2002; Sutton et al., 2011).

Overall, the high rate of HIV infection within young African American MSM is likely a result of factors such as, (a) being less likely to know of their HIV status than other racial groups (Hall et al., 2007; Millet et al., 2007); (b) more likely to have other STIs, which increases the biological possibility and vulnerability for HIV transmission (Wolitski et al., 2001; Millett 2007); (c) restricted sexual networks; (d) a fear of revealing complete sexual behaviors to romantic partners and medical staff ; and (e) once identified as HIV positive less likely to be taking ART than Caucasian MSM (Millet et al., 2007). Moreover, as mentioned above, these factors occur within a socio-cultural context of poverty, poor access to medical treatment, and a high background prevalence of HIV infection among African-American community members.

HIV Treatment

Over the past 25 years, there has been tremendous progress with regard to the treatment of HIV/AIDS; however, there is currently still no cure for this disease (Dinoso et al., 2009). Nonetheless, with proper treatment, many individuals infected with HIV are able to manage their disease as a chronic illness (APA, 2000; Karim et al., 2008; Palmisano & Vello, 2011). At the present time, Antiretroviral Therapy (ART), and more

specifically, the combination of three or more antiretroviral medications (originally known as Highly Active Antiretroviral Therapy [HAART]) has been the standard of care for HIV/AIDS since 1996 (The Antiretroviral Therapy Cohort Collaboration., 2008). All ART is considered "highly active," as national treatment guidelines call for the combination of at least two, but preferably three ARVs (US DHHS, 2012). Therefore, it is not necessary to use the qualifier of "highly active" when referring to ART regimens (S. Hosek, personal communication, May 3, 2012). ART has substantially increased the survival rate and quality of life among individuals living with HIV/AIDS (CDC, 2006; Palella et al., 1998) and is currently the most effective method for treating HIV/AIDS among adolescents and adults (APA, 2000; CDC 2011; US DHHS, 2014). ART regimens, when taken correctly, reduce HIV viral plasma loads to undetectable levels (< 50 m/l), increasing the number and functionality of CD4 T-helper cells, and ultimately restoring the body's immunological functioning (Flynn et al., 2004; Mellins, Havens, McCaskil, Leu, Brudney, & Chesney, 2002; Murphy et al., 2005; Murphy et al., 2001). Moreover, ART is also imperative to HIV prevention efforts, as effective ART significantly decreases the likelihood of HIV transmission to uninfected persons.

ARVs are effective for treating HIV because they are able to block the enzymes that HIV needs in order to replicate. HIV viral replication has multiple steps and ARVs are assigned to different classes of medication based on the step in the HIV viral cycle that they hinder (see figure entitled "Different Classes of Antiretroviral Medications and the Steps in the HIV Viral Production They Thwart" in Palmisano & Vella, 2011). Currently, there are five different classes of ARVs, with each obstructing a different

replication process (Palmisano & Vella, 2011). ART, as a treatment for HIV/AIDS began in 1987 with the introduction of Zidovudine, a medication that thwarts the transcription of viral RNA to viral DNA and falls under the class of nucleoside reverse transcriptase inhibitors (NRTIs; Karim et al., 2008). In 1996, protease inhibitors (PIs) were introduced and proved to be a major breakthrough for HIV/AIDS treatment (Paterson et al., 2000) as PIs stop the gathering of HIV viral offspring within the CD4 + T cell. ART is an aggressive treatment approach in which the individual is prescribed at least three ARVs that comprise of at least one PI or a non-nucleoside reverse transcriptase inhibitor (NNRTI) and two NRTIs (US DHHS, 2011). A combination of ARVs is preferred because it allows for a greater suppression of virus replication (as multiple medications can encumber different processes of viral replication) and an individual is also less likely to build a resistance to ARVs, as they might otherwise develop if they were just using one class of ARVs (Karim et al., 2008; Palmisano & Vella, 2011). Thus, current HIV/AIDS treatment guidelines issued by the United States Department of Health and Human Services advocates for the use of at least two, but preferably three active drugs from two or more classes for treating HIV/AIDS among all adolescents and adults (US DHHS, 2014).

ART Adherence

In order for ART to be effective in reducing HIV viral load and increasing CD4 + T cells, individuals must demonstrate near perfect adherence (APA, 2000; Davies et al., 2006; Paterson et al., 2000; Wutoh et al., 2003). Although, newer research suggests that necessary adherence rates may vary based on class of medication and frequency of

dosage (Maggiolo, et al., 2007). Research groups have most often classified adherence as being the percentage of doses taken within a given time-period (e.g., prescribed doses - missed doses / prescribed doses X 100; Simoni et al., 2006; Williams et al., 2006). Early adherence studies often used an arbitrary adherence cut-off (e.g., taking <80% of prescribed doses) to dichotomize patients as adherent or non-adherent (Bennett, Indyk, & Golub, as cited by Paterson et al., 2000; Wutoh et al., 2003). However, later research indicated that less than a 95% ART adherence rate leads to the progression of HIV viral loads, resulting in higher rates of morbidity and mortality (Murphy et al., 2001; Paterson et al., 2000). Hence, most studies since 2000 conceptualize ART treatment adherence as being 95% or 100% ART adherent (Kahana, Rohan, Allison, Frazier, & Drotar, 2012). In one of the first prospective studies investigating the varying impact of different levels of ART adherence on HIV viral loads, Paterson and colleagues identified that among persons living with HIV who were at least 95% adherent to their medication, virologic failure occurred in only 21.7 % of these patients and the rate of virologic failure increased to 54.6% among individuals who had adherence rates that were only slightly less (90%-94.9%). Moreover, the rate of virologic failure was as high as 82.1% for individuals who took their medication less than 70% of the prescribed doses. Therefore, pharmaceutical companies are currently creating ARVs with longer half-lives which may impact the percentage of adherence that provides optimal virologic outcomes (US DHHS, 2011). Nonetheless, inconsistent ARV adherence can negatively impact one's HIV disease progression and strict adherence to ART is still the number one treatment recommendation for HIV/AIDS (US DHHS, 2014).

Unstable adherence can also lead to the development of ARV resistant strains of the virus, which can deleteriously impact the prognosis of the disease. HIV/AIDS among inconsistent ART adherent patients is more complex and difficult to treat. ARV is less effective for these individuals, as the body develops immunity to these medications (Mehta et al, 1997). Another benefit of being ARV adherent, besides greater mortality and quality of life, is the significantly reduced likelihood of HIV transmission to non-infected persons through sexual intercourse (Palmisano & Vella, 2011). Unfortunately, ART adherence is a major concern among medical providers and HIV/AIDS scientists, as adherence to ARVs is often much lower than what is recommended in order to suppress HIV viral loads to undetectable levels (Chesney et al., 2000; Flynn et al., 2004; Murphy et al., 2001; Murphy et al., 2005; Wutoh et al., 2003). Thus, significant risk exists to both the individual with HIV/AIDS and to the greater public health community. Moreover, medical providers have not been successful at predicting which patients will be ART adherent, which is an additional reason why further research is required in this area (Chesney, 2000; Paterson et al., 2000).

ART Adherence Rates

Overall, the adherence rate for ART is often less than optimal, with many studies commonly classifying less than half of participants as ART adherent (Chesney, 2000; Flynn et al., 2004; Hosek, Harper, & Domanico, 2005; Murphy et al., 2003; Simoni, Amico, Pearson, & Malow, 2008). However, it is important to note that ART adherence rates can vary considerably (e.g., from 20%-100%) depending on adherence rate "cut-off" scores of specific studies (i.e., researchers often dichotomize adherence by a specific

percentage of doses taken within a specified time frame), patient factors, and study methodology (Kahana et al., 2012). For example, Williams and colleagues (2006) reported an ART adherence rate of 84% (when using a 95% adherence cut-off score) in their sample of 1,076 perinatally HIV-infected children and adolescents when using a three-day self-report methodology. On the lower end of the ART adherence spectrum, Flynn and colleagues (2004), reported an ART adherence rate of only 27% (when using a 100% adherence cut-off score) in a sample of 120 adolescents when conducting multiple adherence assessments over a 24-week period (e.g., assessed adherence at baseline and 12 other times). Overall, research indicates that the poor adherence rate for ART is commensurate with adherence to medical treatment for other chronic illnesses (Chesney, 2000).

There are significant medication factor obstacles that hinder successful long-term treatment of this disease. For example, ART regimens have been complex, requiring the management of a high number of daily pills and specific dosage requirements (e.g., timing of pill administration and dietary considerations), consequently making near perfect adherence difficult (Chesney, Ickovics, Hecht, Sikipa, & Rabkin, 1999; Davies et al., 2006; Mellins et al., 2002). Given the poor adherence rates, due to the complexity of ART treatment, pharmaceutical companies are merging multiple drugs into one pill, in order to make treatment easier for patients (Parienti, Bangsberg, Verdon, & Gardner, 2009). For example, Atripla is a single pill that combines three drugs (across multiple classes) for a once a day dosage. Recent research among mostly male MSM older adults, found that individuals on ART once a day doses were less likely to miss a dose compared

to those on multiple pill regimens (Raboud et al., 2011). A prior meta-analysis of once-daily ART found a significant increase of adherence when compared to twice-daily regimens, but at a modest level (2.9% increase in adherence; Parienti, et al., 2009). Although, the advent of a single once-daily pill is promising for reducing ART non-adherence, it also increases the consequences of non-adherence (e.g., HIV viral loads increasing), as the individual is without ARV medication for a longer period of time (Caims, 2010). As the burden of adherence decreases, the severity for non-adherence would rise considerably. Additionally, factors such as patient characteristics, other medication factors (i.e., side effects), severity of disease, and system of care issues have been found to significantly influence adherence to ART among individuals living with HIV/AIDS. Thus, it is important for current and future research to examine which factors play the most important role in ART adherence and for whom, so as to have higher success rates in the treatment of this disease.

As mentioned above, the method of measuring adherence rates has varied among ART adherence studies. Research designs have most often utilized self-report, patient chart review, electronic pill bottle monitoring, and/or a review of pharmacy prescriptions filled to measure ART adherence (Chesney, 2000). The time-period of adherence has also frequently differed between studies with valid arguments articulated for briefer assessment durations (e.g., < than a 3 day recall period) and for longer recall periods (> than 7 days; see Simoni et al., 2006). Because of the aforementioned methodological differences in assessing ART adherence rates (as well as other factors), the percentage of study participants being classified as ART adherent can vary between studies. Hence, the

generalizability across ART adherence studies is somewhat limited. It appears that a self-report method of adherence is the methodology that is most often employed among ART adherence studies (Simoni et al., 2006). Self-report of ART adherence has generally been found to underestimate the rate of ART non-adherence (Ingersoll & Heckman, 2005; Wutoch, 2003). Nevertheless, self-report methodology has been found to be a valid and reliable indicator of medication taking behaviors because of its fairly high correlation with HIV viral load (Ingersoll & Heckman, 2005; Nieuwkerk, & Oort 2005). For example, Simoni and colleagues (2006), conducted a meta-analysis of 77 adherence studies and found self-report of adherence to be strongly associated with other methods of adherence monitoring (among the 27 studies that specifically examined this relationship) and to be predictive of HIV viral load in 84% of the 67 studies reporting this relationship. Other scholars, however, have highlighted the fact that a combination of adherence measurements should be used with self-report (i.e., electronic monitoring, pill count) in order to increase the validity of self-report (Wutoch et al., 2003). However, given the advantages of being an inexpensive method, ease to carry out, and satisfactory predictive and concurrent validity, self-report of ART adherence has been deemed as an appropriate method for measuring ART adherence (Nieuwkerk, & Oort 2005; Simoni et al., 2006; Wutoch et al., 2003).

Predictors of ART Adherence

Given the relatively high rate of ART non-adherence and the considerable public health concern associated with ART non-adherence, scholars have investigated the attributes associated with adhering to ART protocols. As explicated by Chesney (2000),

adherence to ART is most notably affected by patient factors, medication factors, and system of care factors. However, only a few attributes have empirical support for consistently being associated with ART adherence across studies (Ammassari et al., 2002). Individuals living with HIV are a heterogeneous group, and thus research findings have varied based on differences in participant characteristics and study methodology. Hence, ART adherence study results should be interpreted with caution, as research findings do not necessarily generalize to all individuals with the virus. With that being said, the literature has most consistently identified psychological distress, self-efficacy for medication taking behaviors, complexity of medication regimens, and medication side effects as being associated with ART non-adherence (Ammassari et al., 2002; Arnsten et al., 2002; Paterson et al., 2000; Murphy et al., 2001; Murphy et al., 2005; Williams et al., 2006). From a theoretical perspective, it is thought that such attributes may impact individuals' motivation to engage in medication management of a disease (Prochaska et al., 1994). However, even though these attributes have been fairly consistent among research studies, there is still variability with regard to the how these variables predict ART adherence between studies.

Depressive symptoms have commonly been implicated as negatively affecting ART adherence rates across a myriad of patient characteristics (e.g., age, gender, method of infection, and race/ethnicity; Davies et al., 2006; Hosek et al., 2005; Murphy et al., 2001; Phillips et al., 2005; Rao et al., 2007; Williams et al., 2006), but other studies have not found support for depressive symptoms being associated with adherence (Gifford et al., 2000; Rudy, Murphy, Harris, Muenz, & Ellen, 2009). From a theoretical perspective,

the constellation of symptoms associated with depression (e.g., having low motivation, feelings of worthlessness & hopelessness, social withdrawal, lethargy) could have a deleterious impact on a person's ability for self-care (Ingersoll & Heckman, 2005), resulting in a decrease of behaviors needed to adequately comply with ART (e.g., managing medication/leaving the house to acquire medication). In a study of 120 adults with advanced forms of the disease (CD4+ T cell counts below 200), depression was found to increase the risk of running out of medication by threefold (Ingersoll & Heckman, 2005). Some scholars have suggested that the relationship between depressive symptoms and ART adherence may be moderated by gender (Arnsten et al., 2002), with females demonstrating greater depressive symptoms, which inhibit ART adherence behaviors. However, other research has found depressive symptoms to be an important predictor of adherence among studies with predominantly male participants. For example, among 72 participants (88% male) who began ART, depressive symptoms were found to be significantly greater among those who were classified as being non-adherent (Catz, Kelley, Bogart, Benotcoh, & McAulife, 2000). A different study examining adherence to protease inhibitor therapy among 99 patients (96% of which were male), indicated that the presence of depressive symptoms were at least marginally associated with non-adherence (Paterson et al., 2000). As with much of the ART adherence literature, studies examining depression as a predictor of ART adherence is limited by the cross-sectional design of studies, a lack of a gold standard for assessing and measuring adherence, and the use of different instruments assessing depressive symptomology (Ammassari et al., 2002).

Substance use has also been thought to negatively impact the adherence behaviors associated with ART adherence (Hinkin et al., 2004). A recent meta-analysis by Shuper and colleagues (2010), reported that HIV-infected alcohol users are only 47-60% as likely to be ART adherent as non-alcohol users living with HIV. Among 85 adult participants living with HIV, Arnsten and colleagues (2002) found that individuals that actively used cocaine to cope with stress (as opposed to previous cocaine use) were associated with a 41% decline in ART adherence. Cook and colleagues (2001) found a similar decrease in adherence behaviors among "problem drinkers" in their study of 212 patients living with HIV; although, the negative association with ART adherence was not found to be statistically significant (possibly a result of a small sample of problem drinkers 19% of 212 participants). However, "problem drinking" was significantly associated with taking doses at improper times and a greater increase of illicit drug usage (Cook et al., 2001). Other research groups investigating the impact of illicit drug use on ART among an adolescent population found that the age of initial marijuana use is a stronger predictor of ART non-adherence than active marijuana use (Hosek et al., 2005). Scholars have posited that the poor disease progression of individuals living with HIV who are drug users may reflect difference in the use of medical care (Chaisson, Keruly, & Moore, 1995).

Additional attributes that have been found to be associated with ART non-adherence are gender, housing instability, unemployment race/ethnicity, age, socioeconomic status (SES), being on antipsychotic medication, HIV status disclosure, patient attitudes/beliefs, and HIV/medication knowledge, (Ammassari et al., 2002; Mehta

et al., 1997), but findings have been inconsistent across studies (Arnsten et al., 2002; Schneider, Kaplan, Greenfield, Li, & Wison; Williams et al., 2006), suggesting that the relationship between these attributes are likely moderated by other variables being present or controlled for in research designs. For example, some studies have suggested that females are at greater risk for ART non-adherence (Arnsten et al., 2002); while other studies have found that ART adherence differences among gender disappear when appropriate additional variables are accounted for and their effects diminished. For example, previous research has found that women living with HIV were more likely to miss medical appointments than males; however, when childcare was provided during medical visits this adherence discrepancy between genders vanished (Kissinger et al., 1995). Of note, Kissinger and colleagues (1995) defined adherence as the number of missed medical appointments and not actual ART adherence.

In general, less is known about factors that may promote ART adherence or buffer against ART non-adherence in contexts of risk. Only a paucity of factors, such as social support, self-efficacy for taking medication, physician-patient relationship (PPR), and a positive family environment have been indicated to be predictive of ART adherence (Ammassari et al., 2002; Daives et al., 2006; Williams et al., 2006). Self-efficacy for medication taking behaviors is one factor that has consistently been identified as promoting ART adherence (Catz et al., 2000; Gillford et al., 2000) and represents an attribute that may be modifiable by HIV/AIDS intervention and prevention programs. In addition, scholars have investigated the influence of PPRs on ART adherence among individuals living with HIV. In general, physician communication has been established as

being an important factor for medical adherence. A recent meta-analysis conducted by Haskard-Zolnierek, and DiMatteo (2009) investigated the effect of physician communication on adherence to medical treatment among a plethora of studies across patient populations, disease, and settings. This study found that physicians, who were categorized as communicating poorly, had patients who were at a 19% higher risk for poor treatment adherence than patients who reported their physician to be a good communicator. The influence of a positive PPR for individuals living with HIV/AIDS is commonly associated with increased adherence among adult patients (Ingersoll & Heckman, 2005; Schneider et al., 2004). In Beach, Keruly, and Moore's study (2006) of 1,743 HIV positive adults, a single question assessing PPR ("Does your medical provider know you as a person?") was found to predict adherence to ART even when factors such as age, sex, race, and illicit drug use were accounted for (Beach et al., 2006).

Although the research investigating the influence of PPR is promising, little research exists for understanding the benefit among the patients at greatest risk for ART non-adherence (i.e., African-American young males). Research has supported the notion that low-income African-Americans males may have an initial distrust of their physician and medical treatment (Nelson, 2002). An examination of nearly 4,000 individuals over a course of one year, who followed through with prescriptions provided by medical providers (for a variety of ailments) found prescription follow-through to be significantly reduced among low-income African Americans under the age of 65 (Wroth, & Pathman, 2006). Factors that decreased prescription adherence were a lack of confidence in their physician's ability to help and a lack of perceived concern about their medical condition

by their physician. Moreover, research has indicated that African-American MSM living with HIV may present with unique fears (e.g., having their sexual preferences revealed to family members by physicians) and distrust for the medical community that is embedded within a cultural context that highly stigmatizes HIV/AIDS (Kennamer, et al., 2000; Parsons, Cruise, Davenport, & Jones, 2006). Thus, it is important for physicians to be aware of these perceptions and to be cognizant of differing cultural beliefs in order to understand how these fears might impact medical treatment among adolescent and young adult African-American males. The capacity for physicians to become cognizant of how their relationship influences ART behaviors and to subsequently change their patient interaction is promising. For example, Haskard-Zolnierek, and DiMatteo (2009) reported that when physicians are trained to communicate more effectively with their patients, the odds of a patient adhering to medical treatment is 1.62 times greater than when a physician is not trained in effective patient communication.

ART Adherence among Young People

Although scholars have thoroughly investigated ART adherence predictors among adults, our understanding of the issues and factors affecting ART adherence among young people is less developed (Martinez et al., 2000). This is troubling for a number of reasons. First, at least 25% of all new HIV infection cases are among individuals between the ages of 13-24 years-old (CDC, 2011). Secondly, ART adherence among adolescents and young adults is less than optimal (Haberer & Mellins, 2009) and is poorer than adult populations (Becker, Dezii, Burtcel, Kawabata, & Hodder, 2002; Murphy et al., 2003; Raboud et al., 2011; Rao et al., 2007). In the first United States multi-city HIV disease

progression study with adolescents behaviorally-infected with HIV, Murphy and colleagues (2001) reported that only 41% of their sample of 161 adolescents between the ages of 12-18, reported full adherence to their ART regimen. Unfortunately, poor adherence rates among adolescents infected with HIV has been found to be a common occurrence in the HIV literature. Hosek and colleagues (2005), found similar non-adherence rates in their study of 42 HIV infected adolescents (i.e., only 44% were adherent to at least 95% of their ART dosages). Furthermore, prior studies have found that adherence to ART decreases with the duration of use (Martinez et al., 2000). Flynn and colleagues (2004) reported a full adherence rate of only 27% among 120 adolescents over a 24 week period. These authors postulated that the complexity of ART regimes and the requirement of near-perfect adherence rates for ART place adolescents and young adults at a greater risk for non-adherence when compared to other age groups due to their unique behavioral and cognitive circumstances.

Adherence within a developmental framework. The period of adolescence has been identified as a difficult time-period for medical adherence of chronic medical conditions (Rapoff, 1999). Many adolescents have yet to develop formal operational thinking (Piaget, 1963) and the frontal lobe (the area of the brain thought to be responsible for evaluating future consequences of actions and inhibiting impulses) does not reach adult maturity until the mid-20s (Giedd et al., 1999). Thus, adolescents and young adults tend to have more concrete beliefs about the necessity of managing their disease and cannot accurately process the long-term implications of being non-adherent with medical treatments. Socially, adolescents and young adults are particularly

concerned about how their peers view them and they place a greater emphasis on "fitting-in" among their peers than other age groups, as they do not want be different from their peers (Muuss, 1996). Moreover, adhering to ART for adolescents may be especially challenging during asymptomatic phases of the disease, as their adherence to ART can be perceived as a reminder that they are different than their non HIV positive peers (Reisner et al., 2009). Rao and colleagues (2007) conducted a focus group with 25 adolescent/young adults (ages 16-24 years) living with HIV, which highlights the social concerns that these youth have. For example, one participant described being fearful of the disparaging remarks that peers used to identify individuals with HIV (e.g., "he's got the package" p. 31). This can potentially be a devastating barrier for HIV treatment, as adolescents balance the desire to conceal their HIV-status with the necessity of managing a significant number of medical appointments and medications (Chesney, 2000). Simple situations, such as taking medications when at a friend's house, might place adolescents in situations in which they feel vulnerable to being exposed as HIV positive, thus, reducing the likelihood of being ART adherent. During adolescence, parental involvement and family support has been associated with greater medical adherence (LaGreca & Bearman, 2003). However, adolescents and young adults living with HIV from low-income minority communities are often not the recipients of the social support needed to be ART adherent, given the significant HIV stigma within their social networks and the fear associated with family members discovering their HIV positive status (Parsons et al., 2006). Moreover, the social support systems that these youth have available to them are often compromised, as their family members are often burdened

with a high number of significant life stressors (Grant et al., 2000). Therefore, adolescents from low-income minority communities may be motivated to keep their HIV status a secret, in order to protect themselves from the discrimination and potential negative consequences (e.g., being belittled, forced to leave their home) associated with HIV/AIDS (Rao et al., 2007) or may simply may not have social support resources available to them.

Reisner and colleagues (2009) completed a systematic review of all published studies between the years of 1999 and 2008, which focused on ART adherence among youth living with HIV, who were between the ages of 13 and 24 years of age. This review yielded 21 articles and highlighted five broad areas as being important for ART adherence (a) demographic factors; (b) psychosocial factors, (c) disease factors (i.e., HIV viral load, CD4+ T cell count); (d) medication/treatment factors, and (e) physician factors. The following paragraphs discuss important attributes from the aforementioned areas related to ART adherence among HIV positive youth.

Demographic factors. Consistent with the adult ART adherence literature, demographic factors are not often consistent predictors of ART adherence in youth. Inconsistencies have been found for race and gender as a predictor of ART adherence (Reisner et al., 2009). Socioeconomic indicators, such as housing stability (Martinez et al., 2000) and being in school (Murphy et al., 2005) have been associated with increased ART adherence. The most recent published meta-analysis of adherence to ART and virologic responses among children, adolescents, and young adults, reports an equivocal relationship between age and ART adherence (Kahana et al., 2012). For example,

Murphy and colleagues' (2001) large scale HIV disease progression study found no association between ART adherence and age. However, in 2005, when Murphy and colleagues conducted the first longitudinal study of ART adherence with adolescents (which included participants from their 2001 study) they reported younger age as associated with a failure to maintain adherence over a two-year period.

Psychosocial factors. During adolescence and young adulthood, internalizing distress (depressive and anxiety symptoms) has been found to be the strongest and most consistent predictor of ART non- adherence when examining psychosocial factors (Reisner, 2009). The deleterious effect of internalizing distress on ART adherence has been established among both male and female patients and across method of infection (Hosek et al., 2005; Murphy et al., 2001; Murphy et al., 2005; Williams et al., 2006). As mentioned above, the concern of HIV stigma and discrimination from peers has also been found to be associated with ART non-adherence (Martinez et al., 2012; Rao et al., 2007). Low-income African-American young males may be particularly affected by HIV stigma, as their communities view HIV to be a disease of gay men (a behavior that is demonized; Kennamer et al., 2000; Parsons et al., 2006). In addition, the absence of substance or alcohol use has been associated with being ART adherent (Murphy et al., 2005), while earlier age of first marijuana use (Hosek et al., 2005) was found to be predictive of ART non-adherence among samples of youth living with HIV.

Higher levels of self-efficacy for taking ARVs properly and the belief that doing so will lead to an improved quality of life, has been found to be associated with an increase in ART adherence (Belzer et al., 1999; Naar-King et al., 2006). Recent research

has corroborated earlier findings of the beneficial effect of self-efficacy for medication taking behaviors and outcome expectancies on adherence behaviors. For example, a study of 396 patients behaviorally-infected with HIV between the ages of 12-24 years, found that both self-efficacy for medication taking behaviors and outcome expectancies of such behaviors were independently associated with ART adherence (Rudy et al., 2009). Interestingly, general social support has not been found to be an independent predictor of increased adherence among youth living with HIV/AIDS (Naar-King et al., 2006). However, social support geared towards taking ARVs, such as having an adult provide a medication reminder is found to increase adherence (Williams et al., 2006). Thus, social support that is related to medical adherence appears to be an important factor in helping youth achieve ART adherence.

Medication treatment, disease, and physician factors. Medication and treatment regimen factors have been found to negatively impact ART adherence. Most notably, lengths of ARV treatment, medication side effects, and ART complexity (i.e., ART regimens can vary based on a patients response to a certain class of medication and prior ART adherence) all exhibit empirical support for influencing ART non-adherence (Reisner, 2009). Therefore, as mentioned previously, pharmaceutical companies are working to decrease the complexity and side effects of ARVs because adherence to ART is thought to be a life-long treatment for individuals with HIV/AIDS that needs to be built into daily routines (US DHHS, 2014). In addition, to the medication and treatment factors, adolescent and young adults in later stages of the disease are found to be less adherent to ART regimens (Murphy et al., 2005). Unfortunately, the impact medical care

providers may have with regard to ART adherence among youth has not been well investigated. One study did find that regular follow-up care with a treatment provider was associated with improved adherence (Radcliffe, 2006).

Few studies have evaluated theoretical models or frameworks with regard to the interaction of the above said factors and how they ultimately influence ART adherence behaviors for youth living with HIV. In a study of 104, predominately African-American high-risk young youth living with HIV, MacDonell and colleagues (2010) evaluated a Transtheoretical Model for understanding ART adherence. The Transtheoretical model postulates that motivational readiness to change or engage in adherence precedes behavior. In addition, cognitive factors such as self-efficacy and decisional balance (i.e., being able to weigh the pros and cons of a decision) influence motivational readiness, and in turn medication adherence. These investigators found that youth with higher motivational readiness were most likely to have optimal ART adherence. In addition they found self-efficacy and decisional balance to be directly related to each other and motivational readiness. Moreover, social support was found to be related to motivational readiness, but to no other construct. Interestingly, these authors did not find psychiatric illness or substance use to be associated with ART adherence. However, this may be due to the limited variability in these domains within this high-risk sample. Furthermore, there is currently an absence of research investigating how PPR might influence ART adherence in adolescent and young adult populations from minority backgrounds. Little research exists investigating how cognitive factors such as internalizing distress, self-

efficacy, and motivation interact with socioeconomic factors (i.e., housing stability, income, access to health care) in relation to ART adherence.

ART Adherence among African-American Males

As previously stated, African American males constitute the greatest percentage of individuals afflicted with HIV/AIDS, with the majority of these individuals being African-American MSM (Prejean et al., 2011). African-American males have additional barriers to treatment adherence than Caucasians, such as perceived racial discrimination and fear of being stigmatized by their own community for their sexual orientation and HIV status (Bogart, et al., 2010; Hosek et al., 2005; Parsons et al., 2006; Rao et al., 2007). Although research has identified strong predictors of ART adherence among adult African-American male populations, little research has examined the attributes associated with ART adherence among younger African-American males (MacDonell et al., 2010). Studies that have investigated ART adherence among this population have reported an extremely high rate of ART non-adherence. For example, among a diverse group of 42 adolescents (76% African-American, 45% not heterosexual and 60% male with a mean age of 20 years), Hosek and colleagues (2005) reported that only 44% of these were 95% adherent to their ART regimens per their self-report. Martinez and colleagues' (2000) retrospective review of 25 HIV positive youth's medical charts (15 were male and 12 self-reported as MSM) found that an astonishing 80% of male participants were not ART adherent. ART adherence is therefore a prominent concern among young African-American males infected with HIV, but has not been adequately studied by scholars.

The results of Hosek and colleagues' 2005 study indicated negative affect (a variable based on depression/anxiety) and age of first marijuana use as being important predictors of ART non-adherence. Martinez and colleagues (2000) study identified housing instability and greater length of ART as being associated with non-adherence. While these two studies include adolescents at great risk for HIV infection and poor ART adherence (e.g., African-American MSM), they are somewhat limited by (a) extremely small sample sizes; and (b) the examination of only a few factors possibly associated with ART adherence. A notable gap therefore exists in the ART adherence literature with regard to how to successfully manage and sustain ART adherence among this demographic group. It is important for this gap in the literature to be addressed, as young African-American males have disproportionately high rates of HIV infection, poor ART adherence, and poorer HIV disease outcomes when compared to other ethnic groups (Bogart, et al., 2010). Given the severity of consequences for ART non-adherence (e.g., HIV disease advancement, resistance to future antiretroviral medication, greater risk of secondary transmission), it is imperative that scholars understand the factors that both inhibit and increase ART adherence among this population.

CHAPTER THREE

CURRENT STUDY

A large body of literature on predictors of ART non-adherence exists, that being said, there is limited research identifying the factors that predict ART adherence among young African-American males behaviorally-infected with HIV. Furthermore, previous research has clearly identified differential mechanisms or processes of ART adherence among adults infected with HIV based on notable demographic characteristics (i.e., race). The current literature provides limited insight into the demographic, psychosocial, health, and sociocultural factors that may impact ART adherence among adolescent and young African-American males behaviorally-infected with HIV. The lack of ART adherence among individuals living with HIV is a significant public health concern for a number of reasons; (a) ART adherence is the greatest predictor of decreased HIV disease progression; (b) inconsistent ART adherence significantly reduces the effectiveness of ARVs in the future, as the body builds immunity to the medication; and (c) individuals with inconsistent ART adherence, are at greater risk for transmitting HIV to others and transmitting mutated ARV resistant strains of HIV than individuals who are fully adherent with ART.

In view of the aforementioned notable public health concerns and the dearth of research pertaining to understanding what factors are most strongly predictive of ART adherence outcomes among young African-American males behaviorally-infected with

HIV, the current study address this gap in the literature, by identifying the attributes which are the strongest predictors (in that they optimally classify adherence outcomes) of ART adherence among YAAM (between the ages of 12-24 years old), who have been behaviorally-infected with HIV. Given, that little research has examined the predictors of ART adherence among this specific population, it is imperative that this study provide a comprehensive understanding of influences of ART adherence among this "high-risk" group for HIV infection and ART non-adherence. As highlighted in the literature review, there are several notable and consistent predictors (e.g., internalizing distress, self-efficacy, medication complexity) of ART adherence among adults and adolescents with HIV/AIDS, while other predictors appear inconsistent across studies, which is likely a result of varied patient characteristics and study methodology. Furthermore, it is critical to not only identify what attributes predict ART adherence, but how predictors interact among each other, to ultimately influence the pathway towards ART adherence or non-adherence. For instance, Scholars have suggested that predictors of ART adherence interact among each other in complex manners and that the identification of typologies of "adherence" would be beneficial for creating more focused HIV/AIDS intervention and prevention programs (Williams et al., 2006). For example, it has been well-established that individuals living with HIV who also suffer from depressive symptoms are at greater risk for ART non-adherence than individuals living with HIV who do not experience depressive symptoms (Reisner et al., 2009). However, this does not infer that all individuals living with HIV and who experience depressive symptoms will be ART non-adherent. Thus, it is critical to understand what attributes engender additional risk

towards ART non-adherence (i.e., having a substance abuse history, limited social support, low expectations of ARV effectiveness, etc.) and which attributes may offer protection against non-adherence.

Extrapolating from other areas of research examining developmental trajectories, scholars have identified that the occurrence of multiple risk factors in an individual's environment has the greatest predictive power for a negative outcome (Durlak, 1998; Rutter, 1979). In fact, Syndemic theory identifies that the vast number of diseases and social problems are intertwined and interact to increase the negative effects experienced by infected individuals (Klein, 2011). Establishing the pathways towards both adherence and non-adherence in a predictive model for this at-risk group is therefore valuable, as it would allow HIV/AIDS scientists to further understand the pathways toward adherence for this specific demographic group and allow for the creation of more focused and multi-level intervention and prevention programs. In addition, pathways of adherence outcomes may be different between participants who are afflicted by syndemic conditions to a greater degree. Thus, profiles (or the pathways) of adherence are also identified in this high-risk group for HIV infection and poor ART adherence via the use of Classification Tree Analysis (CTA). Medical providers for these individuals will benefit from having an understanding of the profiles of adherence for this at risk-group. ART adherence, like many other human behaviors, is complex, and it is likely that multiple profiles or pathways for engaging or not engaging in such behavior exist. Thus, the identification of ART adherence profiles, will allow medical providers to better identify individuals at

either greater risk or reduced risk for ART non-adherence, and thus, more accurately and appropriately adjust the level of treatment and care needed.

Prior studies investigating predictors of ART adherence have mostly used traditional statistical techniques that limit the number of predictors that can be placed in one statistical model. This is often necessary, as a high number of predictors in one model can greatly reduce statistical power when using conventional statistical techniques (Sieracki, 2010). Therefore, preceding studies have also been limited in the number of possible interactions examined among plausible predictors of adherence. Moreover, ART adherence studies with patient populations that are of interest to the present study (African-American male youth) have been plagued by small sample sizes that notably affect statistical power. Therefore, the limitations of such statistical designs of preceding ART adherence studies among with YAAM, is a restricted understanding of how the many factors in one's life influences the decision of being adherent with ART.

The current study, builds upon the adherence literature by addressing the aforementioned limitations. This is the first study to directly investigate the predictors of ART adherence outcomes, specifically for YAAM behaviorally-infected with HIV, with a large, multisite dataset, from across the US. In addition, this study employs an innovative statistical design, Optimal Data Analysis (ODA), a statistical technique that allows for the inclusion of a vast number of theoretically significant predictors in one statistical model without increasing the risk of statistical error. ODA is superior to other predictive and tree building statistical analyses. For example, no other statistical analysis is better able to maximize the classification accuracy of a dichotomous outcome (Suzuki

et al., 2010; Yarnold & Soltysik, 2005). Other statistical techniques commonly used (e.g., multiple regressions and multivariate analysis of variance) attempt to *maximize a variance ratio*, in order to delineate the average amount of change a specific predictor has on an outcome for the entire study sample, whereas ODA identifies the optimal "cut-point" of an attribute for maximizing the classification accuracy of a dichotomous outcome. ODA is a nonparametric analysis and therefore does not have to meet assumptions of normal distribution. Another notable strength of using ODA for statistical analysis for the present study is the ability to develop an optimal predictive model of ART adherence by creating a classification tree analysis (CTA). A CTA is a nonlinear multi-attribute tree model, which hierarchically maximizes the mean percent accuracy classification of a binary outcome (e.g., adherence or non-adherence). Such an analysis allows for an understanding of what attributes are most important for predicting adherence outcomes, for which members of a sample, and provides an exact cut-off score for each significant attribute. To date, no other research has employed the use of ODA to create a predictive model of ART adherence for YAAM behaviorally-infected with HIV.

Specific Aims

Given the dearth of research examining predictors of ART adherence among African-American adolescent and young adult males behaviorally-infected with HIV, a demographic group at substantial risk for HIV infection and ART non-adherence, the current study addresses this substantial need by (a) identifying the strongest predictor(s) of ART adherence among a relatively large, multi-site sample size of YAAM behaviorally infected with HIV; (b) illustrating the pathways and profiles of ART

adherence for this demographic group; and (c) identifying targets of interventions for future intervention and prevention programs. In order to accomplish these specific goals, the following aims have been put forward.

Aim I: The examination of the most salient predictor(s) of ART adherence among African-American adolescent and young adult males (12-24 years) behaviorally-infected with HIV.

Hypothesis I: Psychiatric illness and more specifically, depressive symptoms are hypothesized to be the strongest predictor of ART adherence among all available attributes.

Aim II: The examination of the pathways and profiles to ART adherence and non-adherence using ODA to construct a CTA model. Specifically, identifying which successive factors maximize classification accuracy of ART adherence outcomes.

Hypothesis II: In the CTA model the attributes of minimal depressive symptoms, age (older participants), self-efficacy for medical adherence, and a positive physician-patient relationship will be the pathway or profile associated with the greatest classification accuracy for ART adherence. Attributes of psychiatric illness, household instability, lower levels of self-efficacy and motivation, and a lack of social support will be the pathway or profile associated with the greatest classification accuracy for ART non-adherence.

Aim III: The identification of protective factors in contexts of increased risk that can be incorporated into intervention and prevention programs aimed at increasing ART

adherence among African-American adolescent and young adult males behaviorally infected with HIV.

Hypothesis III: It is hypothesized that attributes such as mental health treatment, social support, physician-patient relationship, and self-efficacy for medical treatment adherence will act as protective factors and buffer against ART non-adherence in contexts of increased risk for ART non-adherence.

CHAPTER FOUR

METHODS

Participants

Participants were originally recruited from participating sites of the Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) in 2010-2011for a network-wide assessment of current health status and behavioral risk factors among youth living with HIV. This work was supported by the National Institutes of Health through the National Institute of Child Health and Human Development with supplemental funding from the National Institutes on Drug Abuse and Mental Health. Within the larger project (Huszti et al., 2011), a total number of 2,216 adolescents and young adults (age range 12-26 years, M = 20.2 years SD = 2.8 years), 1421 (64.1%) male, 732 female (33.0%), and 56 transgender (2.5%) participated in the protocol at one of the 20 Adolescent Medicine Trials Units (AMTU) across the US and US territories (i.e., Children's Hospital Los Angeles, CORE Center/John Stroger Hospital Chicago, University of Puerto Rico, etc.). The racial composition of participants was 67.0% African-American, 12.5% European-American, 11.1% Multi-Racial, 1% Asian-American or Pacific Islander, 1% Native American, and 6.5% of participants reported racial composition as "other." In the overall sample, 19.7% reported being of Hispanic heritage. Among Hispanic participants, 31.0% reported being Puerto Rican, 20.2% as Mexican/Mexican-American, 19.0% as having a mixed Hispanic background, 8.0% as Dominican, 7.6% as Central American, 3.9% as

South American, 2.8% as Cuban, and the remaining 7.5% identified as "other" or refused to answer. Among all participants, 33.2% were employed, 42.8% were in school, and 83.2% had previously disclosed their HIV status. The vast majority of participants (69.3%) were individuals who reported earning less than $1,000 during the past 30 days.

For the purpose of the current study, a subsample of African-American males behaviorally-infected with HIV, who were currently taking antiretroviral medications (*n* = 387, age range 12-24 years, M = 21.3 years SD = 2.1 years) were included in the analyses. The majority of these individuals identified their sexual orientation as gay (67.7%), bisexual (16.5%), or heterosexual (11.9%), and a small percentage reported "other" or did not answer. Among these participants 44.7% were living with their parents, 28.4% lived in their own house or apartment, 13.4% lived with a relative who was not their parent, 5.7% lived with a non-family member, and the remaining 8.8% reported being homeless or another living situation. Close to half of this study's sample was currently employed (43.7% employed; 56.3% unemployed), yet, 73.6% reported earning less than $1,000 during the past 30 days. Approximately 42.9% were in school, and 86.8% had previously disclosed their HIV status.

Procedures

Individuals living with HIV ages 12 to 24 years-old, who understood written and verbal English, and who received care (minimum of one visit) at one of the 20 AMTU were eligible for participation. Participants were excluded from the study if they exhibited signs that they were unable to complete study measures. For example, participants were excluded based on the presence of serious psychotic symptoms (e.g.,

active perceptual disturbances), suicidal or homicidal ideation, and being intoxicated at the time of consent/assent. AMTU staff enrolled potential participants after obtaining informed consent from the youth, or per local Institutional Review Boards (IRB), parental/guardian permission and assent for youth who were minors. Once enrolled in the study, participants completed demographic, ART adherence, health, psychosocial, and risk-taking behavior measures (described in detail below) in a private room or space via an Audio Computer-Assisted Self-Interview (ACASI) within two weeks of enrollment. After completing the ACASI, participants were debriefed with a face-to-face interview with an AMTU staff member. All ACASI administrations occurred between 2010 and 2011 and were completed in a single visit. Biomedical chart data were collected within one week of the participants' initial visit and included CDC classification for HIV disease, AIDS diagnoses within previous 90 days, non-AIDS diagnoses within previous 12 months, and two year ARV history. In addition, most recent HIV viral load and CD4+T cells count (if collected within the prior six months) was documented. If there was no biomedical chart data within the prior six months for HIV viral load and CD4+ T cell count, a blood sample was collected by AMTU staff.

The original protocol research team completed the appropriate human subjects' safety plan and received (IRB) approval from the appropriate governing institutions. In addition, full IRB approval was obtained from Loyola University Chicago (LUC) prior to data analyses to ensure adherence with LUC's human subjects' safety policies.

Measures

General demographics. Age, marital status, school status, completed education, employment status, total monthly income, living situation, housing stability, access to technology, sexual orientation, age diagnosed with HIV, and HIV disclosure status were determined through a self-report questionnaire on the Audio Computer Self-interview (ACASI) and were included as predictors of ART adherence. Refer to Table 1 for a complete list of all predictors utilized in data analyses.

Mental health. ***Brief Symptom Inventory.*** Mental health functioning was assessed with the Brief Symptom Inventory (BSI), a 53-item self-report measure that consists of three global indices (global severity, positive symptom distress, and positive symptom total), as well as nine primary symptom subscales (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism; Derogatis, & Spencer, 1993). The questionnaire asks participants to rate on a five-point likert scale (from "Not at all" to "Extremely") how much a "problem" has caused distress over the past seven days. The BSI has been shown to be a valid and reliable measure of mental health distress with internal consistency among scales ranging from 0.71 on the psychoticism scale to 0.85 on the depression scale (Derogatis, & Spencer, 1982). Moreover, the BSI has been successfully used among individuals living with HIV/AIDS in a number of prior studies (Kennedy, & Skurnick, 1995; Perry et al., 1993; Reece, Basta, & Koers, 2004). In the current study, the nine BSI scales evidenced appropriate levels of internal consistency, as Cronbach's alpha ranged from 0.74 to 0.87.

Table 1. Predictors of ART Adherence Outcomes Included in ODA

Construct item/scale/subscales	Number of predictors	Predictors
Demographic	15	Age Marital status School status Completed education Employment status Total monthly Income Living situation Housing stability Anticipate moving Sexual orientation Age Diagnosed with HIV Hiv disclosure status Cell phone access Computer with Internet access Email access
Mental health functioning	12	Brief Symptom Inventory (BSI) Global severity Positive symptom distress Positive symptoms total Somatization Obsessive-compulsive Interpersonal sensitivity Depression Anxiety Hostility Phobic anxiety Paranoid ideation Psychoticism
Mental health care utilization (over the prior 12 months)	4	Perceived need for mental health Mental health treatment received Number of times counseling sought Suicidal ideation
Substance use and severity	7	ASSIST (past 3 months freq) Tobacco use Alcohol use Cannabis use Cocaine use Amphetamine use Sedatives use CRAFFT total score
Social support	1	Total social support for healthy living

Construct item/scale/subscales	Number of predictors	Predictors
Self-efficacy		Self-efficacy for medical appointments Self-efficacy for medication routines Total self-efficacy for medical care
Motivation	3	Motivation take meds as prescribed Motivation keep medical appointments Total motivation for medical care
Health care provider relationship	1	Total healthcare provider relationship score
Adherence assessment		
Medication factors	3	Number of daily dosages Daily pill burden Difficulty taking pill
Facilitators to adherence	10	Did something to help remember Labels Calendar Pill boxes Beepers Timers Programmable wrist watches Buddy system Take pills when a certain event occurs Other
Barrier to adherence	13	Experienced difficulty in past 7 days No access at drugstore Prescription elapsed Sickness Forgetfulness Schedule interference Needed break (didn't feel like taking) Living situation change Worried about others finding out Other illness Family/friends don't help remind Reminds me of HIV+ status Other reason
Total number of predictors	72	

Mental health care. Mental health care utilization over the prior 12 months was assessed via self-report. Specifically, participants reported on their desire/need for a mental health professional, actual mental health treatment received, number of mental health treatment sessions received, and if they experienced suicidal ideation over the past 12 months.

Substance use. ***The Alcohol, Smoking, and Substance Involvement Screening Test.*** Substance use during the past three months was assessed with the ASSIST; a 10-item questionnaire that assesses the use of drugs (such as tobacco, alcohol, cannabis, cocaine, amphetamines, inhalants, sedatives, hallucinogens, opioids, and "other substances"), as well as the frequency of such usage with a 5-point likert scale ("Never to "Daily"). The ASSIST was originally developed to assess illicit drug usage by patients in a primary health care setting by the World Health Organization in 1997. The ASSIST has demonstrated strong convergent, construct, predictive, and discriminative validity and is able to discriminate between low, moderate, and high risk substance use (WHO-ASSIST Working Group, 2003). For the current study, each question assessing the severity of usage (during the past 3 months) for a specific substance (e.g., cocaine) was entered as an independent predictor. Individual substances were only entered in the model if at least five percent of the sample endorsed some frequency of use (during the past 3 months).

CRAFFT. The CRAFFT is a six-item self-report measure that assesses consequences for illicit drug/alcohol use, as well as abuse/dependence. Knight, Sherritt, Shrier, Harris, and Chang (2002), demonstrated that the CRAFFT has strong criterion validity among an adolescent clinical population (n = 538) where 75% of participants

were of a racial or ethnic minority group status. A score of two or higher on the CRAFFT predicted strong sensitivity and specificity for problematic drug/alcohol usage and for a clinical disorder. In the current study, a total CRAFFT score was created by collapsing the scores across all six items and demonstrated strong internal consistency ($\alpha = 0.72$).

Social support. ***Social support questions.*** Six questions were included to assess the level of perceived social support in key areas related to medication adherence (i.e., keeping medical appointments, "taking HIV medication", "telling your partner about your HIV status", "using condoms", "avoiding drug use", and "avoiding alcohol use"). Participants' rated their perceived level of social support with a five-point likert scale (from "Strongly Disagree" to "Strongly Agree"). Higher scores indicated stronger perceived social support. For the current study, a total social support scale was created by collapsing the scores across all six questions. Cronbach's alpha = 0.80, indicating an appropriate level of internal consistency among items.

Self-efficacy. ***Self-efficacy for health-care.*** Six questions (3 related to medical appointments; 3 related to medication routine) were administered related to the participants' confidence for keeping future medical appointments and their medication routine. Participants were asked to rate the aforementioned questions with a five-point likert scale (from "Very sure I can" to "Very sure I cannot"). Lower scores indicated a stronger perceived ability to manage their health needs. A previous study with youth of color living with HIV found the self-efficacy for medication routine questions to have adequate reliability (e.g., $\alpha = 0.81$; MacDonell et al., 2010). For the current study, a Total Self-Efficacy Health-Care scale was created by collapsing the scores across all six

questions. In addition, a Self-efficacy for Keeping Medical Appointments scale and a Self-efficacy for Keeping Medication Routine scale were created as well (based on 3 questions each). Cronbach's alphas for the above said scales were 0.80, 0.69, and 0.81 respectively.

Motivation. ***Rollnick's Readiness Ruler.*** Participants were asked to rate on a scale from one ("Not ready") to ten ("Completely ready") their motivation to adhere to take their prescribed medications and make at least four medical appointments per year (Rollnick's Readiness Ruler; Stott, Rollnick, Rees, & Pill, 1995). These two questions of health care motivation were entered as a predictor of ART adherence and in previous research has been recommended for use by clinicians to assess readiness to change for HIV positive individuals (MacDonell et al., 2010). In addition, a total health care motivation item was created by collapsing participants'' responses on the above said questions ($\alpha = 0.64$).

Physician patient relationship. ***Health care provider relationship questions.*** Five questions were included in the overall adherence assessment that focused on the perceived relationship/interaction of the patient with his/her health care provider (e.g., "I feel understood by my care provider"). Participants were asked to assess their perceived relationship/interaction with their healthcare provider with a five-point likert scale (from "Strongly Disagree" to "Strongly Agree"). Higher scores indicated a stronger perceived relationship with their healthcare provider. For the current study, a total healthcare provider relationship scale was created by collapsing the scores across all five questions.

After doing so, the total healthcare provider relationship scale demonstrated an appropriate level of internal reliability ($\alpha = 0.85$).

Adherence. ***Adherence assessment.*** Participants were asked to report the number of missed doses over the last "weekend" and over the last "seven days." A dose was defined as all pills required to be taken at a specific time. The dependent variable for the current study was self-report of adherence over the past seven days. Participants reporting 100% adherence over this time frame were coded as adherent and those reporting missing at least one dose were coded as non-adherent. Nineteen follow-up questions assessing the barriers and facilitators of adherence originally developed for the Reaching for Excellence in Adolescent Care and Health (REACH) study (Murphy et al., 2001) were modified based on findings from Simoni and colleagues' (2006) review of the antiretroviral medication adherence literature. For the purpose of the current study, only adherence questions related to medication factors (e.g., pill burden and number of daily doses) and facilitators (medication reminders) and barriers (recent stressors) of adherence were included as predictors of ART adherence. In addition, only questions that were endorsed by at least five percent of participants were included in analyses.

Data Analysis

A merged dataset containing a network-wide assessment of current health status and behavioral risk factors from the ATN was obtained and cleaned for the purpose of the current study. All aforementioned scales and subscales were created and found to have acceptable internal consistency. Subscales pertaining to BSI variables were only

computed for participants if at least 90% of items were valid. With regard to all other subscales a minimum of 70% was required.

Missing data. Observations with missing data were not imputed, as missing data was a relatively low occurrence. A few question items on the ACASI related to mental health and barriers/facilitators of adherence were not asked of every participant due to skip patterns programmed into the ACASI. Therefore, these items were not imputed as well.

Optimal data analysis. Optimal Data Analysis (ODA) was employed using the ODA software for Windows to identify the attributes with the greatest ability to accurately classify participants as either being ART adherent or ART non-adherent. Theoretically relevant variables (72 in total) from the measures described above (see Table 1 for all variables entered into the ODA model) were entered without selecting explicit predictors or specifying a priori interactions. As described by Snowden, Leon, Bryant, & Lyons (2007), this allowed for the investigation of all possible attributes that may predict ART adherence without increasing error. As instructed by Yarnold and Soltysik (2005), UniODA was conducted for each variable, thus determining which attributes are independent significant predictors for ART adherence outcomes. In addition, a leave-one-out (LOO) jackknife analysis procedure was performed for each attribute to ensure reliability.

ODA was selected for statistical analysis because of the superior benefits that it provides for classifying outcomes compared to other statistical analyses (e.g., discriminant analysis). ODA maximizes classification accuracy of a model for a given

sample of data, provides conceptual clarity, and is easily interpretable. More importantly, ODA is free from meeting the typical assumptions of parametric tests (e.g., normality of distribution, independence, and linearity). In addition, when ODA is used to create Classification Tree Analysis (CTA) models, the assumption that the same attributes are important for all members of a sample does not exist. Rather, ODA is used to identify which attributes are most important for maximizing classification accuracy for different subsets of a sample (Smith et al., 2010).

Classification tree analysis. In addition, to conducting UniODA, hierarchically optimal classification tree analysis (CTA) was performed. CTA is an iterative ODA procedure that allows for the creation of a nonlinear multi-attribute tree model, which hierarchically maximizes the mean percent accuracy classification of a binary outcome (i.e. successive predictors are used to classify with the greatest precision a gradually decreasing amount of the total sample). ODA differs from other statistical designs for creating tree models (e.g., regression tree analyses) in that it does not require distributional assumptions and uses an exact permutation probability to optimally classify outcomes (Yarnold & Soltysik, 2005). Furthermore, traditional statistical techniques presume that the attributes chosen are done so because they are significant predictors for every member of a sample, have the same direction of influence for every member of a sample, and have the same coefficient value for all members of a sample. However, ODA selects attributes based on maximizing classification accuracy of the class variable and therefore, in a CTA model, different attributes classify different subsets of a sample, while labeling groups of individuals that share a common pathway (Smith et al., 2010). In

addition, the same attribute may appear more than once in a model (based on the classification of different subsamples in the model) and both the direction and coefficient of an attribute may also vary for different subsamples of the overall sample (Yarnold & Soltysik, 2005).

To further explicate the CTA procedure, as described in Soltysik and Yarnold (2010), CTA models identify a root node (an attribute that is relevant for all members of a sample) and the ODA algorithm creates a "cut-point," which is the level or point of an attribute that possess the greatest classification accuracy of the class variable. Subsequently, branches or pathways towards classifying members of the sample into different levels of the class variable are formed from the original root node. From the root node other branches originate and continue to do so until the model can no longer increase classification accuracy for the total sample. Branches in the models illustrate pathways and ultimately lead to branch endpoints.

In the current study, an enumerated CTA model was constructed using automated CTA software for Windows. The enumerated CTA model is the most advanced version of CTA and offers several advantages over manual CTA. Specifically, enumerated CTA evaluates a combination of attributes in the top three nodes, selecting the constellation of predictors, which will evidence the greatest effect strength sensitivity (ESS) for maximizing the classification of the class variable (Soltysik & Yarnold, 2010). ESS is a standardized index of effect strength and allows for the direct comparison of ODA models regardless of sample size, number or type of attributes, or number of class categories (Yarnold & Soltysik, 2005). In addition, other notable benefits of CTA include

an automated "pruning" procedure, which prevents the model from over fitting as the model is being created and optimal pruning of the completed model to maximize ESS (Soltysik & Yarnold, 2010). This procedure prevents the CTA model from describing random error instead of the underlying relationship and enhances the overall predictive performance of the CTA model.

Enumerated CTA allows for the development of incredibly granular models, which may result in near perfect classification accuracy. However, these models may have endpoints with small numbers of observations from the larger sample, which can limit the potential generalizability of such CTA models (Yarnold, Bryant, and & Smith, 2013). Thus, in order to prevent the development of too granular of a CTA model for the current study, the CTA program was instructed to maintain a minimum of 10% of the overall sample in each end point.[1] In addition, the CTA program was instructed to only allow attributes in the final CTA model which were LOO stable and to prune attributes from the model with p-values greater than .05. At the current time, there is no "gold-standard" for demarcating endpoint denominators, as such scholars utilizing CTA methodology need to balance perfect classification accuracy with parsimonious and utilitarian models. Therefore, with respect to the current study, the end points minimum of 10% of the overall sample was selected, as this marker adequately balanced the study's objective of creating a CTA model with strong overall effect strength sensitivity for predicting ART adherence behaviors, but that was also parsimonious and generalizable to the larger demographic population.

Lastly, assessing the performance of a CTA model is reliant on several indices as explicated by Soltysik and Yarnold (2010). *Sensitivity* is the likelihood of the model classifying all ART adherent participants as being ART adherent. *Specificity* is the likelihood of the model classifying all ART non-adherent participants as being ART non-adherent. *Positive predictive value (PPV*) is the likelihood that a participant predicted to be a member of the ART adherence group is correctly classified. *Negative predictive value (NPV)* is the likelihood that a participant predicted to be a member of the ART non-adherence group is correctly classified. *Percentage accuracy in classification (PAC)* or "overall accuracy" is the percentage of correctly classified observations in the model. As previously mentioned, *Effect Strength Sensitivity (ESS),* is the statistical index in which all CTA models are evaluated with 0 representing the expected classification accuracy of chance and with 100 representing perfect classification (Soltysik & Yarnold, 2010).

CHAPTER FIVE

RESULTS

Descriptive Analyses

In the current study, the dependent variable was 100% adherence to ART over the past seven consecutive days. Participants who reported not missing a single dose were coded as ART adherent and all other participants were coded as ART non-adherent. In the current sample, 62.3% of participants reported 100% adherence over the past seven days. Means, standard deviations, and/or frequency analyses for all study variables were conducted and can be referenced in Table 2 (Demographic, Mental Health Utilization, & Adherence Characteristics) and Table 3 (Brief Symptom Inventory, Substance Use variables, & Health-Care related Characteristics).

UniODA Analysis

Univariate analysis was conducted with 72 theoretically relevant attributes using ODA (Table 1). Attributes included in the analysis comprised of 12 demographic characteristics, 16 mental health variables, 7 substance use factors, 26 variables assessing perceived barriers and facilitators of adherence, 3 technology access variables, and 8 health-care related characteristics. In total, 28 attributes were significantly associated with ART adherence outcomes (Table 4). Of these 28 attributes, seven (which are identified below) met criteria for meeting the experimentwise type one error rate and the remaining 21 attributes met the generalwise type one error rate criteria.

Table 2. Demographic, Mental Health Utilization, & Adherence Characteristics for African-American Males Behaviorally Infected with HIV 12-24 Years of Age

Demographics	*n* (%)
Age (years)	
M	21.32
SD	2.06
Mdn	22.00
Min	12
Max	24
Current marital status	
Single	337 (87.1%)
Living with a steady partner	39 (10.1%)
Married	3 (0.8%)
Separated	1 (0.3%)
Divorced	0 (0%)
Widowed	0 (0%)
Other	7 (1.8%)
Are you in school these days?	
No	124 (32.0%)
Yes	166 (42.9%)
No, I have graduated	73 (18.9%)
Yes, but I am on summer/winter/spring break now	24 (6.2%)
Highest level of education or grade completed	
Eighth grade or less	6 (1.6%)
More than eighth grade did not complete high school	65 (16.8%)
High school graduate	127 (32.8%)
GED	22 (5.7%)
Some college or technical education or higher	134 (34.6%)
Technical school graduate	11 (2.8%)
College graduate	18 (4.7%)
Some graduate school	4 (1.0%)
Are you currently employed?	
Yes	169 (43.7%)
No	218 (56.3%)
How much money did you make altogether during the past 30 days?	
< $500	98 (25.3%)
$51-$249	69 (17.8%)
$250-$499	53 (13.7%)
$500-$999	65 (16.8%)
$1,000-$2,999	61 (15.8%
$3,000-$4,999	4 (1%)
$5,000 or more	1 (0.3%)
Rather not answer	16 (4.1%)
Don’t know	50 (5.2%)

Demographics	*n* (%)
Where are you currently living or staying most of the time?	
Your own home or apartment	110 (28.4%)
At a parent's house or apartment	173 (44.7%)
At another family member's house or apartment	52 (13.4%)
At a non-family member's house or apartment	22 (5.7%)
Foster home or group home	1 (0.3%)
In a rooming, boarding, halfway house, or a shelter/welfare hotel	18 (4.7%)
On the street(s	3 (0.8%)
Some other places not mentioned	8 (2.1%)
In the last year, how many times have you moved?	
M	1.70
SD	3.44
Mdn	1.00
Min	0
Max	35
How do you identify your sexual orientation?	
Straight	46 (11.9%)
Gay	262 (67.7%)
Queer	1 (0.3%)
Bisexual	64 (16.5%)
Questioning	8 (2.1%)
Other	4 (1%)
Refused to answer	1 (0.3%)
Don't know	1 (0.3%)
HIV/AIDS Related Characteristics	
How old were you when you found out you were HIV positive?	
M	18.74
SD	2.19
Mdn	19.0
Min	5.0
Max	24.0
Have you disclosed your HIV status to anyone?	
Yes	336 (86.8%)
No	51 (13.2%)
Heath Care Utilization	
In the past 12 months, did you want or need help with personal or family problems from a mental health professional such as a social worker, psychiatrist, psychologist or counselor?	
Yes	127 (32.8%)
No	260 (67.2%)

Demographics	*n* (%)
In the past 12 months, have you seen a psychiatrist, psychologist, marriage & family therapist, or social worker about the way you were feeling or behaving (if answer from the above is YES)?	
n	127
Yes	34 (26.8%)
No	
In the past 12 months, how many times have you sought counseling?	
M	1.87
SD	4.73
Mdn	0.00
Min	0
Max	33
In the past 12 months, did you ever seriously consider attempting suicide?	
Yes	51 (13.2%)
No	336 (86.8%)
Adherence Characteristics	
# of daily dosages	
M	1.11
SD	0.38
Mdn	1.00
Min	1
Max	4
Number of daily pills	
M	2.34
SD	1.53
Mdn	2.00
Min	0
Max	8
Pill that is hard to take	
n	366
Yes	25 (6.5%)
No	361 (93.3%)
Adherence Barriers to Adherence	
Did an event occur in the last 7 days that made it more difficult to take your medicine?	
Yes	54 (14%)
No	333 (86%)
No access at drug store	
n	168
Yes	20 (11.9%)
No	148 (88.1%)

Demographics	*n* (%)
Prescription elapsed	
n	166
Yes	42 (10.9%)
No	122 (72.6%)
Sickness	
n	168
Yes	22 (13.1%)
No	
Forgot	
n	168
Yes	120 (71.4%)
No	48 (28.6%)
Schedule interference	
n	168
Yes	25 (14.9%)
No	143 (85.1%)
Didn't feel like taking (needed break)	
n	168
Yes	30 (17.9%)
No	138 (82.1%)
Living situation changed	
n	168
Yes	21 (12.5%)
No	147 (87.5%)
Worried about others finding out	
n	168
Yes	29 (17.3%)
No	138 (82.7%)
Other illness	
n	168
Yes	22 (13.1%)
No	146 (86.9%)
Lack of family support	
n	168
Yes	18 (10.7%)
No	150 (89.3%)
Reminds me of HIV+ status	
n	168
Yes	35 (20.8%)
No	133 (79.2%)

Demographics	*n* (%)
Other reason	
n	168
Yes	34 (20.2%)
No	134 (79.8%)
Facilitators of Adherence	
Use of labels	
n	167
Yes	48 (28.6%)
No	119 (70.8%)
Use of calendar	
n	167
Yes	60 (35.7%)
No	107 (63.7%)
Use of pill boxes	
n	168
Yes	79 (47.0%)
No	89 (53.0%)
Use of beepers	
n	167
Yes	37 (22.0%)
No	130 (77.4%)
Use of timers	
n	168
Yes	62 (36.9%)
No	106 (63.1%)
Use of programmable wrist watches	
n	168
Yes	20 (11.9%)
No	148 (88.1%)
Use of buddy system	
n	168
Yes	58 (34.5%)
No	110 (65.5%)
Take pill when a certain things happens	
n	168
Yes	80 (47.6%)
No	88 (52.4%)
Other	
n	168
Yes	54 (32.1%)
No	114 (67.9%)

Demographics	*n* (%)
Doses missed (past 7 days)	
n	387
0	241 (62.3%)
1	61 (15.8%)
2	42 (10.9%)
3	15 (3.9%)
4+	28 (7.2%)

Note. $N = 387$.

Table 3. Brief Symptom Inventory (BSI) Subscales & Global Indices, Substance Use, & Health Care related Characteristics Descriptives

	M (*SD*)	α
BSI dimensions		
Somatization (7 items)	0.70 (0.78)	0.87
Obsessive-Compulsive (6 items)	1.04 (0.97)	0.87
Interpersonal Sensitivity (4 items)	0.95 (1.03)	0.85
Depression (6 items)	0.95 (0.97)	0.88
Anxiety (6 items)	0.70 (0.85)	0.87
Hostility (5 items)	0.99 (0.97)	0.85
Phobic Anxiety (5 items)	0.54 (0.82)	0.85
Paranoid Ideation (5 items)	1.19 (1.02)	0.82
Psychoticism (5 items)	0.86 (0.88)	0.74
Global indices		
Global Severity Index (GSI) (53 items)	0.89 (0.80)	0.98
Positive Symptom Distress Index	1.72 (0.69)	
Positive Symptom Total (PST) (53 items)	23.52 (14.43)	
CRAFFT		
CRAFFT Total Score (6 items)n =386	2.32 (1.78)	0.72
Car ride intoxicated?	Yes (64.6%)	
Substance use to relax/fit in?	Yes (46.0%)	
Substance use alone?	Yes (49.7%)	
Forgetfulness while using substance?	Yes (27.9%)	
Family concern about substance use?	Yes (27.5%)	
Trouble while using substance?	Yes (16.1%)	
CRAFFT Score > 2 (indicated abuse/dependence)	227 (58.8%)	
Assist		
Current frequency of tobacco use	1.53 (1.76)	
Current frequency of alcohol use	1.51 (1.11)	
Current frequency of cannabis use	1.44 (1.64)	
Current frequency of cocaine use	0.12 (0.50)	
Current frequency of amphetamine use	0.14 (0.48)	
Current frequency of sedative use	0.14 (0.63)	
Motivation Readiness for Healthcare		
Total Motivation (2 items)	19.12 (2.36)	0.64
Motivation for keeping medical appointments	9.57	1.33
Motivation to take HIV medications	9.55	1.41
Self-Efficacy for Medical Care		
Total Self-Efficacy for medical care (6 items)	7.65 (2.32)	0.80
Self-Efficacy for taking medication (3 items)	2.84 (0.97)	0.80
Self-Efficacy for keeping medical appointments (3 items)	3.04 (1.12)	0.70
Social Support for Healthy Living		
Total Social Support for Healthy Living (6 items)	25.75 (4.59)	0.80
Physician-Patient Relationship		
Total Physician-Patient Relationship (5 items)	27.98 (6.13)	0.85

Note. $N = 387$.

Table 4. Univariate Associations of Antiretroviral Therapy Adherence among African-American Males (ages 12-24) Living with HIV

Optimal discriminant analysis			Training analysis		
Attribute	UniODA Model	*N*	% adherent	*p*<	ESS
	Moderate Effect Strength Predictors				
Frequency of cannabis use (past 3 months)	If monthly or more predict non-adherence	144	45.1	0.00	27.1
	If once or twice predict adherence	243	72.4		
Frequency of alcohol use (past 3 months)	If monthly or more predict non-adherence	163	47.2	0.00	27.0
	If once or twice predict adherence	224	73.2		
Crafft Total Score	If score suggestive of substance abuse predict non-adherence	227	52.0	0.00	25.5
	If score does not suggest substance abuse predict adherence	159	76.7		
Frequency of tobacco use (past 3 months)	If monthly or more predict non-adherence	146	47.3	0.00	24.1
	If once or twice predict adherence	241	71.4		
	Relatively Weak Predictors				
BSI Positive Symptom Distress Index	If two or more predict non-adherence	225	53.3	0.00	22.1
	If one or less predict adherence	162	74.7		
BSI Global Severity Index	If "a little bit" or more predict non-adherence	216	53.7	0.00	20.3
	If "not at all" predict adherence	171	73.1		
BSI Positive Symptom Total	If 24 or more predict non-adherence	181	52.5	0.00	19.5
	If 23 or less predict adherence	206	70.9		
Did an event occur that made it more difficult to take medicine (past 7 days)	If yes predict non-adherence	54	31.5	0.00	18.3
	If no predict adherence	333	67.3		
BSI Obsessive-Compulsive Subscale Mean	If "a little bit" or more predict non-adherence	223	55.2	0.00	17.9
	If "not at all" predict adherence	163	72.4		
BSI Hostility Subscale	If "a little bit" or more predict non-adherence	278	56.5	0.00	17.7
	If "not at all" predict adherence	109	77.1		

Optimal discriminant analysis			Training analysis		
Attribute	UniODA Model	*N*	% adherent	*p*<	ESS
"Other" strategy which facilitates Adherence	If no predict non-adherence	114	52.6	0.02	17.7
	If yes predict adherence	54	72.2		
BSI Depression Subscale	If "a little bit" or more predict non-adherence	202	54.5	0.00	17.4
	If "not at all" predict adherence	185	70.8		
BSI Psychoticism Subscale	If "a little bit" or more predict non-adherence	253	56.1	0.00	17.1
	If not at all predict adherence	134	73.9		
Total Self-Efficacy for Medical Care (mean)	If "pretty sure I can" or less predict non-adherence	140	51.4	0.00	16.7
	If "very sure I can" predict adherence	247	68.4		
Current living situation	If living at own place, boarding/halfway house, or homeless predict non-adherence	132	50.8	0.01	16.7
	If living at parents' home, at family members' or non-family members' home, foster home, school dorm, or other place not mentioned predict adherence	255	68.2		
# of total daily pills	If two or more predict non-adherence	204	55.9	0.01	14.3
	If one or less predict adherence	183	69.4		
Total self-efficacy for keeping medical appointments	If "pretty sure I can" or less predict non-adherence	163	54.6	0.01	13.8
	If "very sure I can" predict adherence	224	67.9		
Total self-efficacy for taking medications mean	If "pretty sure I can" or less predict non-adherence	113	51.3	0.01	13.6
	If "very sure I can" predict adherence	274	66.8		
BSI Anxiety Subscale	If "a little bit" or more predict non-adherence	230	57.0	0.03	13.5
	If "not at all" predict adherence	157	70.1		
BSI Interpersonal Sensitivity Subscale	If "a little bit" or more predict non-adherence	159	54.7	0.03	13.2
	If "not at all" predict adherence	228	67.5		

Optimal discriminant analysis			Training analysis		
Attribute	UniODA Model	*N*	% adherent	*p*<	ESS
Total Motivation Readiness for Health Care Mean	If "unsure" predict non-adherence	80	47.5	0.00	13.0
	if "ready & able" predict adherence	307	66.1		
Readiness to take prescription medication	If "unsure" predict non-adherence	55	41.8	0.00	12.4
	If "ready & able" predict adherence	332	65.7		
Age	If 22 years of age or older predict non-adherence	196	56.6	0.04	12.2
	If 21 years of age or less predict adherence	191	68.1		
Is there a pill that is hard for you to take?	If yes predict non-adherence	25	28.0	0.00	9.5
	If no predict adherence	361	64.8		
Frequency of amphetamine use (past 3 months)	If once or twice predict non-adherence	37	40.5	0.00	8.8
	If never predict adherence	350	64.6		
Readiness to go to medical appointments	If "unsure" predict non-adherence	54	48.2	0.03	8.4
	If "ready & able" predict adherence	333	64.6		
Frequency of cocaine use (past 3 months)	If once or twice predict non-adherence	29	41.4	0.02	6.7
	If never predict adherence	358	64.0		
# of daily doses prescribed	If two or more predict non-adherence	33	45.5	0.04	6.1
	If one or less predict adherence	354	63.8		

Consistent with previous literature, the vast majority of statistically significant attributes were in the predicted direction. Four of the 28 significant attributes evidenced moderate effect strength sensitivity (ESS 25-50%) for classifying ART adherence outcomes, while the remaining 24 statistically significant attributes exhibited relatively weak effect strength sensitivity (<25%) for classifying adherence outcomes.

Moderate effect strength. All four attributes that exhibited moderate effect strength sensitivity associated with ART adherence outcomes were variables of participant substance use or abuse and were free from missing data and met experimentwise type one error rate criteria (Table 4). Specifically, the variable with the highest effect strength sensitivity for classifying ART adherence outcomes was frequency of cannabis use during the past three months ESS = 27.1, $p < 0.00$. Participants who reported at least "monthly" use of cannabis during this time period were predicted to be non-adherent to ART (54.9% were actually non-adherent), while those participants who reported cannabis use of less than twice during this time period were predicted to be adherent of their ART regimen (72.4% were actually adherent). In addition, to cannabis use, the substances of alcohol and tobacco were also found to demonstrate moderate effect strength sensitivity for ART adherence outcomes. Specifically, those who reported at least "monthly" alcohol use during the past three months were predicted to be non-adherent to ART (52.8% were actually non-adherent), while those participants who reported alcohol use of twice or less were predicted to be adherent of their ART regimen (73.2% were actually adherent) , ESS = 27.0, $p < 0.00$. The use of tobacco exhibited a similar profile, those who reported at least "monthly" use during the past three months

were predicted to be non-adherent to ART (52.7% were actually non-adherent), while those participants who reported the use of twice or less were predicted to be adherent of their ART regimen (71.4% were actually adherent), ESS = 24.1, p <0.00. Lastly, participants who scored as likely to have a substance abuse problem (on the CRAFFT) were predicted to be non-adherent to ART regimens (48% were actually non-adherent), while those who scored in the non-substance abuse range were predicted to be ART adherent (76.7% were actually adherent), ESS = 25.5, p <0.00. Overall, variables that exhibited moderate effect strength sensitivity associated with ART adherence outcomes were all related to substance use. Moreover, for all of these variables greater use was significantly associated with non-adherence, while the absence of monthly use or the likely absence of substance abuse was associated with a greater likelihood of being ART adherent.

Relatively weak effect strength. In total, 24 out of the possible 72 attributes exhibited a significant, but relatively weak, effect strength sensitivity associated with ART adherence outcomes (Table 4). The majority of these attributes were mental health characteristics, followed by perceived barriers and facilitators of adherence, health care self-efficacy and motivation related factors, demographic characteristics, and additional substance use variables.

Mental health characteristics. The most notable mental health characteristics associated with ART adherence outcomes were those which measured global symptom severity, as well as total positive symptom distress, as measured by the Brief Symptom Inventory (BSI). Of note, the variable of total positive symptom distress met the

experimentwise criteria for type one error rate. Participants who evidenced greater symptom distress were associated with ART non-adherence, while those who reported lower levels of symptom distress were associated with ART adherence. In addition, this pattern was demonstrated for several individual subscales on the BSI. Specifically, those participants who endorsed a mean symptom score equivalent to or greater than "a little bit" associated with the BSI subscales of obsessive-compulsive, hostility, depression, anxiety, interpersonal sensitivity, and psychoticism were associated with ART non-adherence, while those participants whose mean score was equivalent to "not at all" were associated with ART adherence (Table 4).

Barrier and facilitator characteristics. There were a number of factors that are perceived barriers or facilitators of ART adherence, which were significantly associated with ART adherence outcomes. The strongest association was related to the presence or absence of an event (during the past 7 days) that made it more difficult for the participant to take his medicine. The presence of such an event was associated with ART non-adherence (68.5% were actually non-adherent), while the absence of such an event was associated with ART adherence (67.3% were actually adherent) ESS = 18.3, $p < 0.00$ and met the experimentwise criteria for a type one error rate. Participants who endorsed having a pill that is hard to take were associated with ART non-adherence (72.0% were actually non-adherent), while those who did not perceive having difficulty taking a pill were associated with ART adherence (64.8% were actually adherent) ESS = 9.5, $p < 0.00$ and this attribute met the expereimentwise type one error rate criteria. In addition, the level of pill burden was significantly associated with ART adherence outcomes.

Specifically, two or more daily pills and two or more daily doses were associated with ART non-adherence, while one daily pill and dose was associated with ART Adherence. Lastly, having a reminder strategy for taking medication was associated with adherence outcomes. Participants who reported not having a strategy were associated with ART non-adherence (47.5% actually were non-adherent), while those reporting have such a strategy were associated with ART adherence (72.2% actually adherent), ESS = 17.7, $p<0.03$. Of note, this factor only had 168 valid cases out of 387 cases.

Health care efficacy and support characteristics. In general, participants who evidenced lower levels of self-efficacy related to managing their medical care were associated with ART non-adherence, while those who reported higher self-efficacy for managing their medical care were associated with ART adherence. For example, those who reported being "pretty sure" or less, with regard to managing their medical appointments and medication were predicted to be non-adherent to ART (48.6% were actually non-adherent), while those participants who reported being "very sure" were predicted to be adherent of their ART regimen (68.4% were actually adherent), ESS = 16.7, $p <0.00$. In addition, participants' motivation to engage in health care (e.g., take medication & keep medical appointments) was significantly associated in the expected direction. That is, those who reported lower levels of motivation were associated with ART non-adherence, while those who reported higher levels of motivation were associated with ART adherence.

Demographic characteristics. Among all demographic characteristics, two were significantly associated with ART adherence outcomes. The strongest association

exhibited related to current living situation. Specifically, those participants who reported living at their own place, at a boarding place, or being homeless were predicted to be ART non-adherent (49.2% were actually non-adherent), while those who reported either living with family, a foster home, school dorm, or another place were predicted to ART adherent (68.2% actually were adherent), ESS = 16.7, $p < 0.02$. Age was also associated with ART adherence outcomes. Participants 22 years of age or older were associated with ART non-adherence (43.4% were actually non-adherent), while participants 21 years of age or younger were associated with ART adherence (68.1% actually adherent), ESS = 12.2, $p < 0.05$.

Substance use characteristics. In addition, to the substance use variables that demonstrated moderate effect strength associations with ART adherence outcomes, two additional substance use variables evidenced a weak effect strength sensitivity association with ART adherence outcomes. For both amphetamines and cocaine, the use of "once or twice" during the past three months was associated with ART non-adherence, while the absence of amphetamine and cocaine use during this duration was associated with ART adherence.

Classification Tree Analysis

The enumerated CTA yielded an overall model (Figure 1) that delivered moderate effect strength sensitivity (ESS = 38.0%) for classifying participants, as either being ART adherent or non-adherent. Thus, the model provides a 38% improvement above chance for classifying members of the sample, as either being ART adherent or non-adherent.

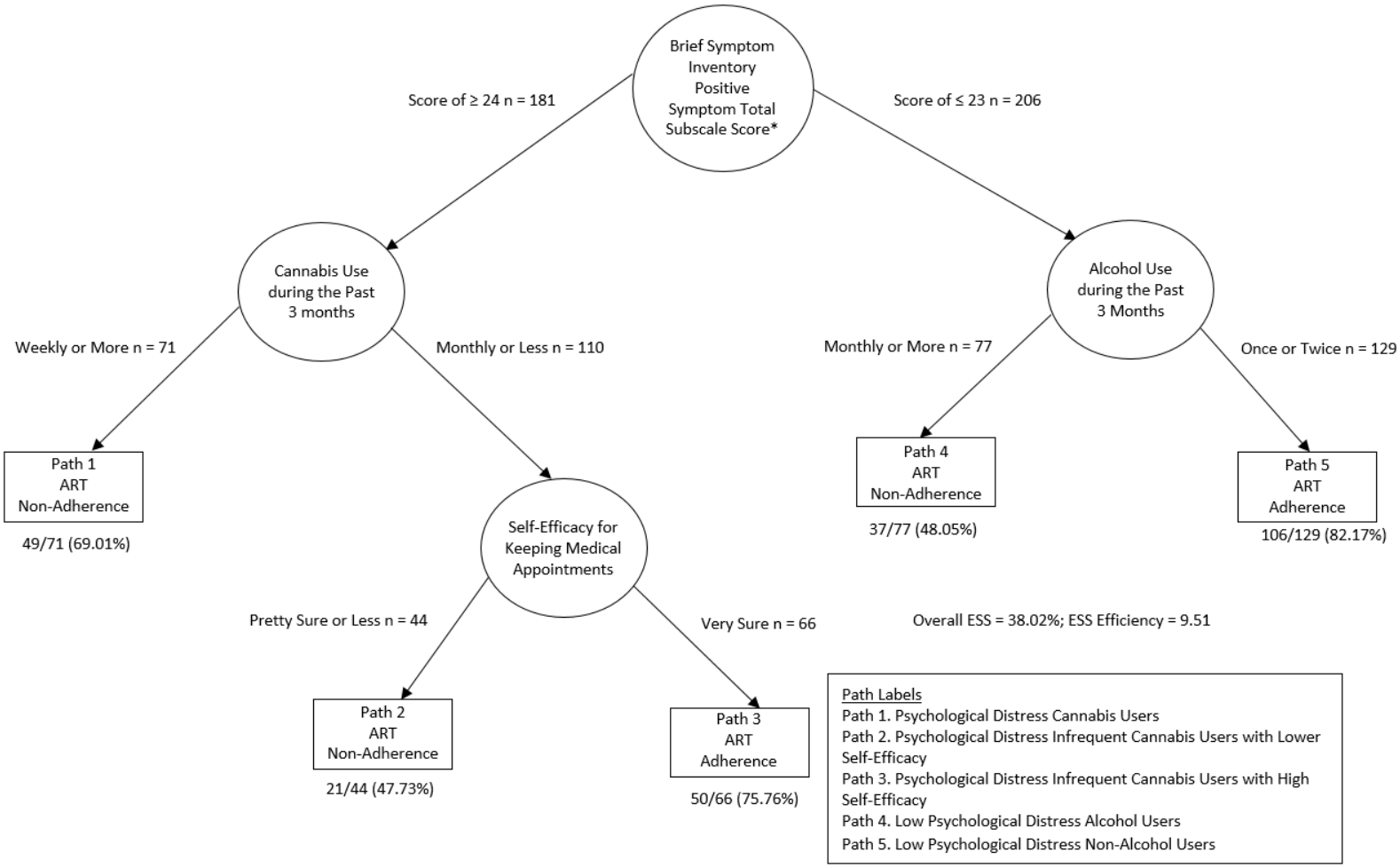

Figure 1**.** CTA Model for Classifying ART Adherence and Non-Adherence. *n* = 387. *BSI PST Subscale Score Range = 0-53.

The CTA model correctly classified 73.3% of all participants who were ART non-adherent and 64.7% of all participants who were ART adherent, with an overall PAC mean of 68%. In addition, 80% of participants predicted to be ART adherent were indeed adherent, while only 55.7% of participants who were predicted to be ART non-adherent actually were non-adherent (see Table 5 for complete CTA model performance statistics). As illustrated in Figure 1, the CTA model identified three profiles or pathways of ART non-adherence and two profiles of ART adherence with respect to the current sample.

Table 5. ART Adherence Classification Tree Model Performance Summary

Performance index	Performance parameter
Sensitivity	156/241 (64.7%)
Specificity	107/146 (73.3%)
Positive predictive value	156/195 (80.0%)
Negative predictive value	107/192 (55.7%)
Overall accuracy (PAC)	263/387 (68.0%)
Effect strength sensitivity	38.0% (Moderate Strength)

ART non-adherers on Path 1, "Psychological Distress Cannabis Users," endorsed a positive response on at least 24 of the 53 items on the BSI subscale of Positive Symptom Total (BSIPST [$M = 35.70$, $SD = 8.23$]) and reported at least weekly use of cannabis during the past three months (see Table 6.). The mean use of cannabis for this group however, was approaching "almost daily" use ($M = 3.72$, $SD = 0.45$). Pathway 1 yielded the highest PAC for classifying ART non-adherers at 69% (49/71). ART non-adherers on Path 2, "Psychological Distress Infrequent Cannabis Users with Lower Self-Efficacy," endorsed a positive response on at least 24 of the 53 items of the BSIPST ($M = 37.68$, $SD = 8.60$), but reported only monthly or less use of cannabis ($M = 0.66$, $SD = 0.78$), and only being "pretty sure" or less that they could keep future medical

appointments $M = 2.04$, $SD = 0.41$). Pathway 2 yielded a PAC of only 47.7% (21/44) for predicting ART non-adherence. The final ART non-adherence pathway (Path 4) yielded a PAC of 48.1% (37/77). ART non-adherers on Path 4, "Low Psychological Distress Alcohol Users," endorsed 23 or less of the 53 items on the BSIPST ($M = 13.56$, $SD = 8.36$) and reported monthly or more alcohol use ($M = 2.68$, $SD = 0.60$) during the past three months (refer to Table 6).

Table 6. Descriptive Information of CTA Model Pathways

Pathway	BSIPST[a]	Cannabis use	Alcohol use	Self-efficacy[b]
Path 1. Psychological distress cannabis users	$M = 35.70$ $SD = 8.23$	$M = 3.72$ $SD = 0.45$	$M = 2.00$ $SD = 1.06$	$M = 1.35$ $SD = 0.44$
Path 2. Psychological distress infrequent cannabis users with lower self-efficacy	$M = 37.68$ $SD = 8.60$	$M = 0.66$ $SD = 0.78$	$M = 1.66$ $SD = 1.08$	$M = 2.04$ $SD = 0.41$
Path 3. Psychological distress infrequent cannabis users with high self-efficacy	$M = 36.76$ $SD = 8.37$	$M = 0.33$ $SD = 0.59$	$M = 1.18$ $SD = 1.05$	$M = 1.10$ $SD = 0.15$
Path 4. Low psychological distress alcohol users	$M = 13.56$ $SD = 8.36$	$M = 1.56$ $SD = 1.56$	$M = 2.68$ $SD = 0.60$	$M = 1.24$ $SD = 1.49$
Path 5. Low psychological distress non-alcohol users	$M = 11.16$ $SD = 6.80$	$M = 0.96$ $SD = 1.49$	$M = 0.67$ $SD = 0.47$	$M = 1.23$ $SD = 0.40$

Note. $n = 387$.

[a] BSIPST = Brief Symptom Inventory Positive Symptom Total Subscale Score

[b] Lower scores = higher levels of self-efficacy

Two distinct ART adherence pathways were identified in the CTA model. ART adherers of Path 3, "Psychological Distress Infrequent Cannabis Users with High Levels of Self-Efficacy," possessed similar characteristics to ART non-adherers in Path 2, but

differed in their level of self-efficacy for keeping future medical appointments (refer to Table 6), as these participants reported being "very sure" that they could keep such appointments. ART adherers in Path 3 yielded a PAC of 75.8% (50/66). The second and final pathway of ART adherence was Path 5, "Low Psychological Distress Non-Alcohol Users," such participants endorsed 23 items or less of the 53 items on the BSIPST (M = 11.16, SD = 6.80) and reported alcohol use of just once or twice during the past three months (M = 0.67, SD = 0.47). This pathway yielded the greatest PAC of ART adherence, as 82.2% (106/129) of those predicted to be ART adherent were adherent.

As identified in the Attribute Importance in Discrimination (AID) analysis (refer to Table 7), BSIPST (a measure of mental health), was involved in classification decisions for all 387 participants. Furthermore, level of substance use was also involved in classification decisions for all 387 participants. Alcohol Use was involved in all classifications on the right-hand side of the root attribute (BSIPST; 387-181 = 206), thus, influencing classification decisions for 53.2% of the overall sample. On the left-hand side of the BSIPST attribute, cannabis use was involved in all classification (387-206 = 181), influencing classification decisions for 46.8% of the overall sample. Lastly, in the CTA model Self-Efficacy for Keeping Future Medical Appointments influenced 28.4% of the total sample. In addition, post-hoc descriptives were conducted for each of the five pathways identified in the final CTA model (See Table 6).

Table 7. Attribute Importance in Discrimination Analysis for ART Adherence

	Amount of sample evaluated in part on basis of attribute	
Attribute	#	%
BSIPST[a]	387/387	100.0
Alcohol use	206/387	53.2
Cannabis use	181/387	46.8
Self-efficacy for keeping medical appointments	110/387	28.4

[a] BSIPST = Brief Symptom Inventory Positive Symptom Total.

CHAPTER SIX

DISCUSSION

The development and improvement of antiretroviral therapy (ART) has afforded individuals living with HIV/AIDS an opportunity to live significantly longer and healthier lives than before treatment was available. Adherence to ART protocols has been strongly associated with reduced secondary transmission of HIV, reduced likelihood of virus mutations, increased immunological functioning, slowed disease progression, and increased life expectancy (CDC, 2006; Flynn et al., 2004; Mellins et al., 2002; Palella et al., 1998). That being said, the benefit of ART is directly contingent upon an individual's ability to adhere to it daily. Given the high adherence rate requirement (>95%) for optimal outcomes, this poses a significant challenge, as it has been well documented in the literature that many individuals struggle with adherence to ART regimens.

Thus the purpose of the current study was to advance the ART adherence literature by identifying the strongest predictors and profiles of ART adherence and non-adherence among a "high-risk" population; adolescent and young adult African-American males (YAAM) behaviorally-infected with HIV. In the United States, this demographic group has been infected with HIV at disproportionally higher rates than other demographic groups and in recent years the rates of new HIV infections among this group have risen dramatically (Prejean et al., 2011). However, limited research exists pertaining to the complex ways in which demographic, health, psychosocial, behavioral,

and sociocultural variables may influence ART adherence behaviors among this demographic group, despite their significant risk for both HIV infection and poor ART adherence. Thus, the present study begins to fill this void, by exclusively investigating the predictors of ART adherence among a large, multi-site sample of young African-American males (YAAM) behaviorally-infected with HIV. This study employed Optimal Data Analysis (ODA), a statistical analysis which maximizes classification accuracy, to identify both the strongest predictors of ART adherence outcomes and the specific profiles of adherence behaviors among this population.

In general, partial support was found for the study's hypotheses. The first hypothesis was that psychiatric illness, and more specifically depressive symptoms, would be the strongest predictor of ART adherence outcomes among all attributes in the model. UniODA analysis identified depressive symptoms as being a significant predictor of ART adherence outcomes, but the main effect was relatively weak. In addition, global indices of psychological distress and the number of self-reported symptoms (across psychological domains) were found to have stronger effect strength sensitivity (approaching moderate effect strength) for predicting ART adherence behavior than depressive symptoms alone. When investigating the main effects of all attributes in the model, UniODA analysis identified that the strongest predictors of ART adherence outcomes, were all related to substance use. Specifically, monthly use of cannabis, alcohol, and tobacco during the past three months, as well as the likelihood of an individual having a substance abuse issue (as measured by the CRAFFT) all evidenced moderate effect strength sensitivity for predicting ART adherence outcomes.

Interestingly, when the enumerated classification tree analysis (CTA) was conducted, with the goal of increasing classification accuracy for ART adherent outcomes, the total number of self-reported psychological symptoms on the Brief Symptom Inventory (BSI) was found to be the optimal root attribute for differentiating between participants who were ART adherent and those who were non-adherent. Thus, although, substance use variables were consistently found to be the strongest predictors of ART adherent behavior when examining main effects, when constructing the CTA model, psychological symptom total as the root attribute, led to the most accurate model when including multiple attributes hierarchically to predict adherence outcomes. This highlights the notable role of global psychological distress and underlines the importance of not only focusing on the impact of internalizing distress (i.e., depression and anxiety) on ART adherence outcomes, but to also have an appreciation for overall mental health functioning across psychological and emotional domains and how these impact ART adherence behaviors.

The study's second hypothesis postulated what attributes would account for the profiles and pathways of ART adherence and non-adherence. Specifically, it was hypothesized that individuals in the sample who evidenced minimal depressive symptoms, who were older, possessed high levels of self-efficacy related to medical adherence, and who had a positive physician-patient relationship would most likely demonstrate ART adherence. Conversely, it was hypothesized that profiles of ART non-adherence would consist of psychiatric illness or distress, housing instability, lower levels of self-efficacy and social support. Once again, partial supports for these hypotheses were

found. As illustrated in the CTA model (refer to Figure 1), the group of participants most likely to be ART adherent (Path 5 - Low Psychological Distress Non-Alcohol Users), were those who reported fewer psychological symptoms, but who also reported minimal alcohol use during the past three months (e.g., just once or twice). Approximately 82% (106/129 participants) of these individuals, who were predicted to be ART adherent over the past seven days, were in fact adherent. Furthermore, the profile associated with the greatest percentage of ART non-adherent participants, as hypothesized, were participants reporting greater levels of psychological distress. Specifically, participants who reported a higher number of psychological symptoms, as measured on the BSI, and who used cannabis on at least a weekly basis were ART non-adherent 69% (49/71 participants) of the time (Path 1 - Psychologically Distress Cannabis Users).

Lastly, the study's third hypothesis posited that attributes such as mental health treatment, social support, physician-patient relationship, and self-efficacy for medical treatment adherence would act as protective factors in contexts of increased risk for ART non-adherence. Partial support for this hypothesis was found as well. The CTA model identified that self-efficacy (related to keeping future medical appointments) may have a protective role for those at risk for ART non-adherence. As indicated in Figure 1, participants who reported higher numbers of psychological distress symptoms (and are therefore at increased risk for ART-non-adherence) and who used cannabis monthly or less, but, who also exhibited the highest levels of self-efficacy for keeping future medical appointments were found to be ART adherent approximately 76% (50 out of 66 participants) of the time (Path 3 - Psychological Distress Infrequent Cannabis Users with

High Self-Efficacy). Conversely, yet consistent with the study's hypotheses, counterparts who exhibited similar characteristics as participants in Path 3, but who evidenced lower levels of self-efficacy, were ART adherent only 52% (23/44 participants) of the time (Path 2 - Psychological Distress Infrequent Cannabis Users with Lower Self-Efficacy). This equated to a reduction in the percentage of those ART Adherent of over 25% when compared to participants in Path 3. In sum, the results indicate that higher levels of self-efficacy played an important role in adherence among participants with higher levels of global psychological distress and monthly or less cannabis use.

Of note, although one of the primary purposes of this study was to identify protective factors of ART adherence behavior, the CTA model also identified a noteworthy risk factor. Analyses showed that alcohol use (at least monthly) significantly reduced the proportion of participants who were engaging in ART adherent behavior. Specifically, a 30% reduction in the proportion of participants who were ART adherent was found. For example, as illustrated in the CTA model (Figure 1), only 52% of participants (40/77) who were in Path 4 (Low Psychological Distress Alcohol Users) were actually ART adherent, compared to the participants in Path 5 (Low Psychological Distress Non-Alcohol Users) which showed that 82% of participants (106/129) were ART adherent. The only attribute in the CTA model distinguishing between these two groups was the level of alcohol use reported during the previous three months. Post-hoc analysis identified that the vast majority of participants in Path 4 reported between monthly and weekly alcohol use, while the vast majority of participants in Path 3 reported alcohol use of less than once or twice during the past three months (see Table 6).

The study therefore highlights the important role that alcohol use plays in whether an individual will be adherent or non-adherent.

As outlined above, the final CTA model (Figure 1) identified five distinct profiles of ART adherence outcomes. Two profiles identified the pathways predicting ART adherence and the remaining three profiles identified pathways predicting ART non-adherence. However, it should be stated that two of the profiles associated with non-adherence correctly classified ART adherence outcomes at the rate of chance. However, in the context of the overall model, these two non-adherent profiles identified attributes that may act as risk factors for ART adherence (e.g., alcohol use). Each of the five profiles of ART adherence outcomes is outlined below, first for ART adherence behaviors and then for ART non-adherence behavior, in the order of highest classification accuracy obtained in the final CTA model (Figure 1).

Profiles of ART Adherence Behavior

Path 5: Low psychological distress non-alcohol users (profile of adherence). In the current study, Path 5 represented the pathway with the greatest likelihood of engaging in 100% ART adherent behavior (82% [106/129] of participants in this path were ART adherent). These individuals reported low levels of total psychological symptoms and were engaged in minimal alcohol use during the past three months (see Table 6). Therefore, in the current sample of YAAM behaviorally-infected with HIV, the greatest likelihood for ART adherence was among those who reported both minimal global mental health distress and near absence of alcohol use. This constellation of participant characteristics was found to be the most predictive of ART adherence in the

context of a vast number of other competing predictors. Thus, emphasizing the importance of healthy psychological functioning and refraining from substance use for YAAM behaviorally-infected with HIV with regard to adhering to ART.

Path 3: Psychological distress infrequent cannabis users with high self-efficacy (profile of adherence). Participants in the current study who exhibited greater levels of psychological distress were initially predicted to be ART non-adherent. However, as elucidated in Figure 1, there was a significant three-way interaction among the attributes of total number of psychological symptoms, frequency of cannabis use, and self-efficacy. Specifically, participants who were predicted to be ART non-adherent based on their total number of psychological symptoms reported, but who refrained from frequent cannabis use, and who had high levels of self-efficacy for keeping medical appointments were generally found to be ART adherent (76% of participants). Such findings highlight the potential protective role that self-efficacy for engaging in medical care may have with regard to ART adherence behaviors among YAAM behaviorally-infected with HIV.

Profiles of ART Non-Adherence Behavior

Path 1: Psychological distress cannabis users (profile of non-adherence). The final CTA model evidenced greater difficulty expounding the profiles of ART non-adherence with greater accuracy than chance. However, the model did identify one robust profile of ART non-adherence behaviors. Specifically, participants who reported a greater number of psychological symptoms (across psychological domains) and who used cannabis weekly or more during the past three months, were the participants who were

the least likely to demonstrate ART adherent behavior in the final CTA model (Figure 1). Moreover, Path 1, which consisted of higher levels of psychological distress comorbid with frequent cannabis use, was found to be a more accurate predictor of ART non-adherence than the main effects of these attributes alone. For instance, the statistically significant main effect of the total number of reported psychological symptoms only accurately classified 47.5% of participants predicted to be ART non-adherent, while the main effect of frequency of cannabis use during the past three months performed a little better (54.9%), but was still far below the 69% correctly classified when the CTA model combined such characteristics.

Path 1 unequivocally underscores the deleterious influence that comorbid psychological distress and frequent cannabis use for YAAM behaviorally-infected with HIV can have with regard to ART adherent behavior. In the CTA model, no other constellation of attributes was found to be a more accurate pathway for correctly classifying participants as being ART non-adherent. This profile of ART non-adherence behavior (Psychological Distress Cannabis Users) can allow primary care providers a method to identify the patients among YAAM behaviorally-infected with HIV with the greatest likelihood to struggle with ART. As such, primary care providers will be better able to identify patients who are at notable risk for ART non-adherence and can allocate the limited, but necessary resources to help these youth engage in ART more effectively.

Path 4: Low psychological distress alcohol users (profile of non-adherence). By itself, the profile of "Low Psychological Distress Alcohol Users" did not perform better than chance for discriminating between those who were ART adherent and those

who were not. However, in the context of the overall CTA model, this pathway identifies the moderating effect of alcohol use for participants with lower levels of psychological symptoms and ART adherence. Thus, alcohol use (and likely the use of other substances) represents a notable decrease for ART adherence, even among those who report low levels of psychological distress. The moderating effect of alcohol use, suggests the need for primary care teams to further assess for substance use among patients who are not endorsing high number of psychological symptoms, with regard to additional risk for ART non-adherence.

Path 2: Psychological distress infrequent cannabis users with lower self-efficacy (profile of non-adherence). Participants of Path 2, reported high levels of psychological symptoms, infrequent cannabis use (monthly use or less), and lower levels of self-efficacy for keeping future medical appointments. In the CTA model, these participants were predicted to be ART non-adherent. However, only 48% of these participants were indeed ART non-adherent. Although, this Path did not evidence a high degree of classification accuracy, it demonstrated that lower levels of self-efficacy are associated with reduced ART adherence, especially among YAAM with greater psychological distress. In the CTA model, participants in Path 2 only differed from participants in Path 3 (as previously discussed above), in their level of self-efficacy to keep future medical appointments (see Table 6). Yet, there is a considerable decrease in the proportion of participants who were ART adherent going from 76% (in Path 3) to only 52% (in Path 2); a reduction of nearly 24%. Thus, in the context of the overall CTA model, Path 2 highlights the benefit of higher levels of self-efficacy for keeping future

medical appointments for ART adherent behaviors, in particular, for participants with higher levels of psychological distress.

Overall, this study clearly identifies robust pathways of ART adherence outcomes for YAAM behaviorally-infected with HIV. Furthermore, in the current analysis, the grouping of mental health and substance use attributes were found to have the strongest classification accuracy for predicting ART adherence outcomes than any other grouping of other theoretically relevant variables available (i.e., housing stability, social support, motivational readiness, etc.). Such findings speak to the strong influence that mental health and substance use factors have for ART adherence behaviors among this population. In addition, the model identified the potential protective role that self-efficacy for medical care engagement may have with regard to promoting ART adherence behavior for those at increased risk of ART non-adherence. Yet, the protective advantage offered by self-efficacy may be limited in contexts of increased risk (i.e., high levels of cannabis use).

As identified earlier, the CTA model performed with greater accuracy for predicting which participants would be ART adherent versus which participants would be ART non-adherent. Interestingly, the two profiles that did not perform better than chance for predicting ART adherence outcomes were profiles of ART non-adherence. Nonetheless, these less impressive non-adherent profiles (with regard to classification accuracy) in the CTA model still identified attributes, which may function as significant risk factors, thwarting optimal adherence outcomes. For example, participants who reported lower levels of psychological distress were predicted by ODA to more likely be

ART adherent. However, the relationship between psychological distress and ART adherence was moderated by the frequency of alcohol use during the past three months. Thus, although these less accurate pathways may not clearly identify patients as likely to struggle with ART adherence, the pathways do identify characteristics which may reduce the likelihood of successful ART adherence.

The question arises as to why predicting ART non-adherence accurately might be more challenging than predicting ART adherence. Research has identified medical knowledge and a clear understanding of the treatment regimen, as being critical for adherence to medical care (Martin, Williams, Haskard, & DiMatteo, 2005). In addition, these authors note the importance of transparent and effective communication between medical personnel and their patients, as well as the significance of the physician-patient relationship. Although, this study was able to include a measure of physician-patient relationship, it was limited by ceiling effects and this study lacked information on participants' knowledge of HIV/AIDS, or ART. Furthermore, research has indicated that asymptomatic medical conditions are associated with higher levels of non-adherence (Latif & McNicoll, 2009). It is plausible, that in the current study there was a greater degree of variability with respect to symptoms associated with HIV between adherent and non-adherent groups. However, this data was not available. Research in the larger medication adherence literature estimates that there are 100 to 250 various factors associated with non-adherence, many related to behavior and cognitions (e.g., low faith in medication benefit, amount of effort to access medication, fear of stigmatization) that vary greatly among individuals (Bosworth, 2012). Thus, future research among YAAM

living with HIV should explore the set of cognitions that may partially explain thought processes that impede ART adherence for this population.

Taken together, factors leading to accurately predicting ART non-adherence will inherently be more challenging because of these idiosyncratic reasons, compared to the factors which are associated with ART adherence behaviors. For ART non-adherent behaviors, there may be a myriad of factors that potentially differ between individuals, thus making it difficult to amass a large number of individuals into specific pathways or profiles of ART non-adherence. Whereas, those who are able to be adherent may share a common motivation of remaining healthy and have a psychosocial environment that supports this quest.

Results within the Context of the Previous Literature

To date, few studies have specifically investigated the predictors of ART adherence for youth living with HIV. Moreover, even less research has been conducted examining this relationship for YAAM behaviorally-infected with HIV, a group who has been greatly affected by the HIV/AIDS pandemic. In 2005, Murphy and colleagues published the first longitudinal study examining the predictors of ART adherence among an ethnically diverse adolescent population, who were behaviorally-infected with HIV. These authors found lower levels of alcohol use and being in school to be associated with ART adherence. ART non-adherence in this sample was associated with greater levels of depressive symptoms and younger age. Murphy and colleagues' findings were generally consistent with another large scale, multi-site sample, of 253 ethnically diverse youth who were behaviorally-infected with HIV. Specifically, Comulada and colleagues (2003)

found recent substance use to be a significant predictor of ART adherence and that those who reported being adherent to ART, were less likely to have been sexually abused, to have attempted suicide, and to report lower life satisfaction. In addition, "non-adherers" were more likely to engage in negative coping styles (i.e., depression withdrawal & self-destructive escape) than "adherers." Subsequent research has consistently identified the negative impact of psychological distress with regard to ART adherence outcomes (Hosek et al., 2005; Naar-King et al., 2006; William et al., 2006) and higher levels of internalizing distress (i.e., depression and anxiety) have been found to be reliable predictors of poor adherence outcomes (Reisner et al., 2008).

There is a great need for large sample studies investigating the specific influences of ART adherence among YAAM living with HIV, but few exist. One of the larger such studies, is a recent randomized controlled trial of 86 newly diagnosed HIV positive African-American MSM from Project nGage. The findings from this study were strongly commensurate with the current findings. Specifically, these researchers found that ART adherence was associated with less alcohol use, as well as lower desire and compulsions for alcohol (Bouris et al., 2013). In addition, ART adherence was negatively associated with psychological distress. The present study therefore builds upon the ART adherence literature in a noteworthy manner since no study has previously examined the predictors of adherence specific to YAAM behaviorally-infected with HIV with a large multi-site sample. In addition, this study identifies that for YAAM behaviorally-infected with HIV, psychological distress and substance use have stronger associations with adherence

behaviors than other theoretically relevant attributes and should therefore be key areas of focus for comprehensive HIV care for this population.

A significant strength of this study was the ability to include a large number of theoretically relevant attributes in one statistical model, which has allowed for a deeper understanding of how such factors interact to ultimately influence ART adherent behaviors. In the current study, many of the factors (i.e., depressive symptoms, substance use, motivation, etc.) that the previous literature has identified as being associated with ART adherence behavior were found to have significant main effects. However, by using ODA, this study was able to evaluate how robust of a predictor each statistically significant variable was for classifying ART adherence outcomes. Among all 72 predictors in the current study, when examining main effects, substance use attributes demonstrated the greatest effect strength for accurately classifying ART adherence outcomes. However, the deleterious effects of substance use was increased when comorbid with greater levels of global psychological distress. These findings therefore provide strong empirical support for the robust influence of mental health and substance use characteristics with regard to ART adherence behaviors for YAAM behaviorally-infected with HIV.

Recent research by MacDonell and colleagues (2010) posited a cognitive framework for understanding the underlying mechanisms associated with ART adherence behaviors among adolescent and young adults of color living with HIV. These investigators argued that motivational readiness is what drives ART adherence behaviors and cognitive variables, such as decisional balance (being able to reason the costs &

benefits of behavior change) and self-efficacy directly influences motivational readiness. These scholars found that among their sample of 104 participants, those who reported higher levels of motivational readiness were likely to have optimal adherence. In their path model, higher levels of self-efficacy and decisional balance (at a trend-level) were related to higher levels of motivational readiness, which was directly related to increased adherence. In addition, higher levels of social support were directly related to increased motivational readiness and indirectly (at a trend-level) related to adherence. Unexpectedly, these authors did not find a relationship between psychological functioning or substance use for ART adherence behaviors. This is surprising, given that mental health and substance use variables have been consistently found to be associated with ART adherence, as indicated by Reisner and colleagues' (2008) review of published ART adherence studies of youth. In addition, the present study found that such attributes (i.e., mental health and substance use) have the greatest accuracy for classifying ART adherence outcomes. However, MacDonell and colleagues posited that the high levels of mental health distress among their sample and the fact that substance use did not vary by adherence status may have been related to the lack of association between psychological functioning, substance use, and ART adherence.

In the present study, the core mechanisms that explain how attributes in the CTA model influence ART adherent behaviors were not directly investigated. This study does not shed light on the mechanistic relationship between mental health, substance use, and ART adherence for YAAM behaviorally-infected with HIV. However, as postulated by MacDonell and colleagues (2010), substance use may be directly related to ART non-

adherence, but it is likely that underlying cognitive processes, such as motivational factors or self-efficacy, may explain such relationships. In fact, other prominent studies in the literature have identified a number of cognitive variables, such as self-efficacy and the perception of the effects of ARVs (Belzer et al., 1999; Naar-King et al., 2006), as being related to ART adherence behaviors. Further research is therefore necessary to understand the mechanistic properties of notable factors such as substance use and mental health functioning and how they influence ART adherence outcomes. For instance, the direct use of drugs or having significant psychological distress may result in increased forgetfulness, a life style characterized by a lack of structure or organization, social isolation, and/or diminished mental capacity to manage one's own medical needs.

Key Areas of Focus

The results of the current study and prior literature highlight several important areas of focus, in which scholars, interventionists, and primary care providers are encouraged to invest continued energy and critical inquiry, in order to fully understand the psychosocial and health needs of YAAM behaviorally-infected with HIV.

Substance use. Issues of substance use are common among individuals living with HIV and significantly impact an individual's ability to manage their HIV care effectively (Gonzalez, 2011; Strauss et al., 2009). In general, substance use has been found to be associated with poorer adherence to ART, as well as accelerated disease progression, independent of ART adherence (Baum et al., 2010). In the current study, six of the seven substance use variables were found to exhibit statistically significant main effects for classifying ART adherence behaviors. In the final CTA model (Figure 1), the

frequency of alcohol or cannabis use during the past three months were significant predictors for discriminating between adherence outcomes for all 387 study participants (Table 7). Moreover, although previous research has often investigated the influence of substance abuse or dependence (Gonzalez et al., 2011) with regard to ART adherence behavior, the current study identifies that even levels of substance use lower than the criteria for a substance abuse disorder may have a detrimental influence on ART adherence behaviors among YAAM behaviorally-infected with HIV.

While monthly alcohol use may not be seen as "problematic," or inherently thought of as being a risk factor for ART non-adherence, previous literature has recorded that even low levels of alcohol use can negatively impact HIV medical care. For example, in a large-scale study investigating the impact of alcohol use for ART adherence among West-African adults living with HIV, any alcohol consumption within the past year was associated with an increased risk for ART non-adherence (Jaquet et al., 2010). In addition, relatively low levels of alcohol use have also been found to impact adherence to HIV medical care among youth of color living with HIV. For example, Outlaw and colleagues (2010) found that in their sample of 82 youth living with HIV that only alcohol use (as an individual attribute) predicted HIV medical care appointment adherence and that the vast majority of participants reported alcohol use (during the past 3 months) varying from none at all to less than weekly. Thus, in corroboration with the previous literature, this study's finding highlights the significance that even relatively low levels of alcohol use may act as a significant risk factor for ART non-adherence behavior among YAAM behavioral-infected with HIV.

Interestingly, substances that may be thought of as relatively benign (e.g., tobacco) were found to be significant predictors of ART adherence outcomes in the current study and in the prior literature (Shutter, & Bernstein 2008). This is noteworthy, as rates of tobacco use are significantly higher among those living with HIV (50-74%; Reynolds, 2009; Webb, Vanable, & Carey, 2007) versus those who are uninfected (18.1%; CDC, 2014). The treatment of common recreational drugs use such as tobacco, alcohol, and cannabis is likely to be lower on a primary care provider's treatment list when providing medical care for individuals living with HIV, but such substance use has been related to several negative health outcomes for those living with HIV, such as non-AIDS defining cancers, cardiovascular disease, bacterial pneumonia, and increased mortality rates (even when controlling for ART adherence and viral load; Gonzalez et al., 2011).

Taken together, medical providers providing care to YAAM living with HIV should be keenly aware and cognizant of the impact that even low levels of substance use may have on ART adherence behaviors. As such, it would be highly beneficial to include screenings of substance use behaviors and offer appropriate treatment as part of routine care for these individuals, in order to monitor/reduce a notable risk factor for ART non-adherence. Moreover, the development of smoking cessation programs and other programs targeting the reduction of substance use in the primary care setting will likely be vital components for successful and comprehensive HIV medical care. Previous scholars, such as Strauss and colleagues (2009) have proposed the need for primary care providers to be educated in screening and brief intervention for substance use, along with

increasing providers' self-efficacy for implementing such type of treatment, in order for such programming to be successful.

Mental health. The literature examining the relationship between mental health and ART adherence behavior has frequently focused on the influence of internalizing distress (i.e., depression and anxiety). However, given the results of the current study, primary care providers, interventionists, and scholars should be aware that global psychological distress may influence adherence behaviors to even a greater degree than depressive or anxiety symptoms alone for YAAM behaviorally-infected with HIV. As previously mentioned, it is plausible that greater psychological distress across psychological and emotional domains has cumulative or multiplicative effects on daily functioning and may be more taxing on an individual's ability to cope. These findings therefore suggest the importance of developing and providing primary care settings with interventions that help individuals effectively manage global psychological distress, in order to increase the likelihood of successful ART and overall health. A number of cognitive-behavioral interventions geared towards adults and adolescents living with comorbid depression and HIV have been found to be effective in reducing depressive symptomatology (Safren et al., 2012) and increase ART adherence (Daughters, Magidson, Schuster, & Safren, 2010; Safren et al., 2009). Intervention programs would likely benefit from other psychological evidence-base treatment techniques such a motivational interviewing and coping skills training to address psychological concerns other than internalizing distress (i.e., anger, substance use, and emotional dysregulation). For example, in the current study, higher levels of aggressiveness and interpersonal

hostility were found to be significant predictors of ART non-adherence when examining main effects alone.

Comorbid psychological distress and substance use. In the current study, the presence of comorbid mental health distress and cannabis use was the strongest profile of ART non-adherence. Prior research has reported that substance use and mental health disorders co-occur in approximately 23% of individuals living with HIV (Gonzalez et al., 2011). However, these statistics only identify individuals who meet the criteria for a DSM-IV-TR diagnosis and the rates of comorbid substance use and sub-clinical levels of psychological distress are likely greater. Participants who receive HIV care in primary settings, who exhibit elevated, but not clinically significant levels of mental health distress, or those who are engaging in substance use, but do not meet criteria for substance abuse or dependence may not be considered at additional risk for ART non-adherence by primary care providers. However, the current study suggests that such individuals should be treated as "at-risk" for ART non-adherence. Thus, this may require integrated multidisciplinary treatment team models, which can identify even sub-clinical levels of mental health distress or substance use and as a result provide appropriate care for these issues.

Interestingly, this study's findings that comorbid psychological distress and substance use decreases the likelihood of ART adherence to a greater degree than either psychological distress, or substance use are highly consistent with the previous literature (Chander et al., 2009; Mellins et al., 2009). In the current study, increased cannabis use was a stronger predictor of ART non-adherence for those with higher levels of

psychological distress than increased alcohol use. Conversely, increased alcohol use was a stronger predictor of ART non-adherence for those with lower levels of psychological distress than increased cannabis use. However, the previous literature is less clear as to why specific substances have a greater or reduce impact on adherence in the context or absence of mental health distress. Interestingly, with regard to alcohol use, the reduction in ART adherence is likely related to cognitive mechanisms. There is a growing literature that supports the notion that individuals who drink alcohol believe there is a possibility for a negative drug interaction with their ARVs so they refrain from their ARVs when consuming alcohol (Kalichman et al., 2009). Moreover, cognitive-behavioral and psychoeducation interventions have been found to increase ART adherence among individuals living with HIV with comorbid alcohol use (Velasquez, Stemberg, & Johnson, 2009). Despite this, future research expounding upon as to why specific substances generate increased risk in the absence or presence of mental health distress is necessary.

Self-efficacy. In addition to the most salient profiles of ART adherence behaviors previously discussed, primary care providers and interventionists should also be aware of potential protective factors of ART adherence. In particular, attention should be given to the role in which self-efficacy for engaging in medical care may have for ART adherence behaviors for YAAM behaviorally-infected with HIV. In the current study, greater levels of self-efficacy for keeping medical appointments was found to be a protective factor for those with greater global psychological distress, but was moderated by cannabis use (i.e. those engaging in cannabis use monthly or less were more likely to be ART adherent, but

those with greater levels of cannabis use were not). This finding may reflect the potential limitations of self-efficacy with regard to ART adherence behavior in the context of syndemic conditions. A syndemic is two or more public health epidemics (e.g., substance use, HIV, & psychiatric illness), which interact synergistically and are mutually reinforcing, resulting in an excess burden of a disease in a population (Blank & Eisenberg, 2013). For example, in contexts where there are syndemic conditions (i.e., Path 1 – psychological distress & frequent cannabis use), increased self-efficacy for medical care engagement may not provide the protective function for ART adherence that it does for individuals who do not share such conditions (e.g., psychological distress but infrequent cannabis use). It is thought that syndemic conditions are likely responsible for the disproportionate high number of HIV infection among MSM (Talman, Bolton, & Walson, 2012; Herrick et al., 2013). From a syndemic framework, self-efficacy (for keeping future medical appointments) may function as what Luthar, Cicchetti, and Becker, (2000) describe as "protective but reactive" attributes. That is, self-efficacy may generally provide benefit, but less so when other risk factors are high. It is therefore plausible that higher levels of cannabis use, or the interaction of cannabis use and mental health distress may negatively impact an individual's ability to (a) be receptive to messages promoting self-efficacy, or (b) that high levels of self-efficacy may not have the same protective function when multiple risk factors exist.

Previous research with youth living with HIV, has found self-efficacy to be a critical component for successful ART adherence (Naar-King et al., 2006; MacDonell et al., 2010). However, it is important to further investigate for whom greater levels of self-

efficacy are particularly beneficial and if there are limitations of self-efficacy as a mechanism for driving adherent behaviors. For example, in syndemic conditions, it may be critical to simultaneously address other factors (e.g., substance, & mental health distress) before individual's may be responsive to self-efficacy messages. Hence, the importance of medical care providers and interventionists to be cognizant of including the components of substance use reduction, psychological health, and self-efficacy for medical care as part of treatment and intervention efforts for the purpose of increasing ART adherence behaviors.

Cultural and developmental considerations. Research has identified the importance of understanding the developmental and sociocultural milieu of patient populations and how such factors influence health care engagement and health outcomes. YAAM living with HIV may have limited experience in medical or health care settings (prior to their HIV diagnosis) and may lack the confidence, trust, or knowledge to actively engage in their own medical care. Furthermore, research shows that African-Americans as a race have an extensive history of mistreatment by healthcare systems and as a result have higher levels of medical care mistrust than other racial groups (Brandon, Issac, & LaVeist, 2005; Boulware, Cooper, Ratner, LaVeist, & Powe, 2003). Primary care providers working with YAAM living with HIV should be sensitive of how the above said cultural factors influence self-efficacy for medical care engagement and physician-patient relationships. Thus, medical care providers would benefit from being aware of and working to reduce higher levels of medical mistrust as it may be a barrier to effective HIV medical care.

From a developmental perspective, the period of adolescence and emerging adulthood is associated with greater substance use and peer pressure than other development periods (Muus, 1996). The National Longitudinal Study of Adolescent Health reported that rates of alcohol, tobacco, and cannabis use significantly increase from early adolescence to the mid-20s (Chen & Jacobson, 2012). High rates of substance use have been reported for youth living with HIV (Etzel, Lightfoot, Rotheram-Borus, & Swendeman, 2002) and among MSM (Gonzalez et al., 2011). In addition, the rates of substance use among young adults are significantly higher among individuals from low socioeconomic backgrounds than individuals from intermediate or high socioeconomic backgrounds (Redonnet, Chollet, Fombonne, Bowes, & Melchior, 2011). These findings hold true even when controlling for an impressive number of demographic, family background, and juvenile characteristics. Therefore, as a demographic group, YAAM behaviorally-infected with HIV are at a significantly increased risk for substance use.

As alluded to above, Kalichman and colleagues (2009) explicate how the thought processes of substance users may be one mechanism that explains the relationship between substance use and ART adherence behaviors. For example, these authors found that participants who wanted to consume alcohol stopped taking their medications because they believed the mixture of alcohol and their HIV medications could be toxic. However, there is no evidence that suggests mixing alcohol with ARVs provides greater danger/impairment than the alcohol itself (Lowry, 2012); yet, this information is generally unknown by patients receiving HIV care (Kalichman et al., 2009). The pressure to not take HIV medication in lieu of consuming alcohol may be more difficult for

adolescents and young adults, where peer pressure to engage in substance use is often greater than among adult populations (Muss, 1996). In addition, as stated above, the rates of recreational drug use are higher during adolescence and emerging adulthood than in other development periods (Chen & Jacobson, 2012),which increases the overall likelihood that substance use will negatively impact ART adherence among youth living with HIV. Medical professionals providing treatment to such youth should be keenly aware of the likely increase rates of substance use among this population, how such behaviors negatively impacts ART adherence, and the interventions that can be utilized to identify and reduce substance use.

Strauss and colleagues' (2009) study of seven hospital-based HIV care centers in New York City strongly advocates for the necessity of educating HIV primary care providers on the negative effects of alcohol use on disease outcomes, providing patients with education about using alcohol with ARVs, as well as the importance of providing non-judgmental patient treatment settings to discuss obstacles with regard to ART adherence (e.g., substance use). This is likely especially important for young males of color living with HIV, who may be particularly aware of discrimination based on race and sexual preferences. A recent qualitative study of young African-American MSM living with HIV highlighted the need for holistic resilience-based interventions focusing on the developmental and cultural needs of youth transitioning to adulthood (Hussen et al., 2014). These types of treatment settings and interventions would allow primary care providers to educate patients about how substance use may impact ART, allow providers to disconfirm beliefs and myths about the toxic interaction of alcohol and ARVs, discuss

barriers to ART, and devise a plan for successful ART. However, a necessary first step to achieve this type of treatment setting is to increase medical care providers' self-efficacy for discussing patient substance use reduction and cultural factors influencing treatment (Strauss et al., 2009).

Clinical Implications

The findings of the current study can be utilized by primary care providers working with YAAM behaviorally-infected with HIV to improve patient care and ART adherence outcomes. This study suggests that by understanding a patient's current psychological functioning and substance use profile, medical care providers can increase their acumen for identifying which patients may struggle or do well with ART. In particular, this study identified two strong and recognizable profiles or pathways associated with ART adherence behaviors for YAAM behaviorally-infected with HIV. For this demographic group, patients who exhibited low levels of psychological distress and who are not engaging in alcohol use, have a greater likelihood of successfully adhering to ART. Conversely, medical providers should understand that the profile with the greatest likelihood of ART non-adherence, among this same demographic group, are individuals who are experiencing higher levels of mental health distress and who are engaging in frequent cannabis use. Such individuals should be identified by primary care providers as individuals at greater risk for ART non-adherence than peers without such characteristics, and as a result, greater levels of intervention resources may need to be allocated for such patients. The assessment of psychological functioning and substance use, as part of routine care in HIV treatment settings, may have the potential to identify

those at risk for ART non-adherence and provide targeted interventions for these individuals. The current study therefore shows that it is imperative that HIV treatment for YAAM behaviorally-infected with HIV include mental health care and substance use education and treatment. In addition, this study establishes the potential benefit of fostering greater levels of self-efficacy for medical care engagement with regard to ART adherence behaviors. Thus, having medical providers thinking thoughtfully and implementing methods to increase levels of self-efficacy (for engaging in medical care) for YAAM behaviorally-infected with HIV would likely be of great benefit.

The current study elucidates a clear decision making process and screening tools that can be used to identify those at increased risk for ART non-adherence vs. those who likely have a greater chance to be adherent to ART. Specifically, HIV primary care settings providing care to YAAM living with HIV are encouraged to include the Brief Symptom Inventory (BSI; Derogatis, & Spencer, 1993) and the ASSIST (WHO-ASSIST Working Group, 2003), as part of their routine health screening, to assess current mental health symptoms and substance use. Those individuals who score a 24 or higher on the BSI Positive Symptom Total and are engaging in weekly or more cannabis use are those at appreciable risk for ART non-adherence and higher level of intervention will be necessary to help these individuals adhere to ART regimens. In addition, the absence of substance use (e.g., alcohol, cannabis, and tobacco) as well as minimal psychological distress symptoms increases the confidence that youth will be successful with respect to ART adherence.

Integrated case management care models. Given the strong empirical support for the influence of psychosocial variables for ART adherence behaviors among youth living with HIV, it behooves primary care HIV treatment settings to have multidisciplinary treatment teams, consisting of providers with expertise in infectious disease, psychological functioning, substance use, and case management. The treatment of HIV should not solely focus on the pathogenesis of the disease, but should also include a great emphasis on psychosocial functioning as well, as such factors greatly impact patients' ability to tolerate and effectively participate in ART. For example the co-occurrence of HIV, depression, and substance use has consistently been found to be associated with decreased ART adherence (Cook et al., 2001; Gonzalez et al., 2011) and an increase in sexually-transmitted diseases among adult populations (Shoptaw, Peck, Reback, & Rotheram-Fuller, 2003). Moreover, longitudinal research has identified the accelerated decline of HIV viral load, CD4 count, and subsequent mortality for individuals living with comorbid HIV and depression, even when controlling for ART adherence (Ironson et al., 2005). Therefore, in order to successfully treat individuals living with HIV, it is critical to provide care for mental health and substance use as well.

Integrated multidisciplinary behavioral health teams, which practice within a developmentally and culturally sensitive manner, are likely to be best prepared to address the factors influencing ART adherence behaviors for YAAM living with HIV. It is plausible that mental health care and issues of substance use may be over looked or minimized in treatment settings dedicated to the treatment of HIV, given the severity of the disease. However, this study unequivocally demonstrates the significant role of both

mental health and substance use for ART adherence behaviors for YAAM behaviorally-infected with HIV. Therefore, these psychosocial factors should be focal points of HIV treatment teams and interventions. In addition, it is important to note that in the present study, predictors of adherence outcomes were associated with current functioning (i.e., current number of psychological symptoms, current substance use). Thus, the assessment or treatment of psychosocial factors should not only occur during the intake of new patients, but should be an integral part of routine and continued care. Lastly, integrated primary care teams should strongly consider how to increase patient self-efficacy for medical care engagement, as increased levels of self-efficacy in this study and in prior research has been found to be particularly important for youth living with HIV with regard to ART adherent behaviors.

Intervention/Prevention Programs

HIV intervention/prevention programs developed for YAAM behaviorally-infected with HIV are likely to be most successful when developed from cultural and developmentally appropriate frameworks. With regard to YAAM behaviorally-infected with HIV, Harper (2007) argues for the need of HIV intervention/prevention programing to be "culturally-grounded" by including elements of both societal-level and individual-level factors. For example, important components of such programming would include elements of sexual culture for gay and bisexual males, masculinity ideology, sexual identity, and ethnic identity. Interventions that are based in the "real-world" experience of gay youth of color and speak to their values and norms will likely have a greater chance of being successful than interventions that do not integrate such content. Thus successful

ART adherence interventions for this population would benefit from being created in a "culturally-grounded" manner, in addition to being based in the "real-world" experience of youth living with HIV.

As MacDonell and colleagues (2010) have previously articulated, successful intervention and prevention programs must target the large range of factors that influence ART adherence behaviors. These include cultural, developmental, societal-level, psychosocial, and individual level factors. Thus, multifaceted behavioral interventions presented within developmentally and culturally sensitive frameworks are likely to be the most successful for increasing ART adherence behaviors among youth behaviorally-infected with HIV, as well as reducing the rate of new HIV infections in "at-risk" communities. Given the results of the current study, HIV intervention and prevention programming for YAAM behaviorally-infected with HIV would likely benefit from including core components related to healthy psychological functioning, substance use reduction, psychoeducation with regard to HIV pathogenesis and health management, coping skills, and increasing self-efficacy for engaging in medical care.

Research shows that CBT-based interventions have been found to be efficacious for increasing ART adherence among adult populations (Daughters et al., 2010), as well as among HIV positive adult alcohol users (Parson et al., 2007). In addition, a randomized controlled trial of CBT combined with psychoeducation, problem-solving techniques, and cognitive restructuring skills has demonstrated being effective for reducing depressive symptoms and increasing ART adherence among individuals living with HIV (Safren et al., 2009). Moreover, these investigators found these significant

changes to generally have been maintained at six-month and twelve-month follow-up points. Thus, indicating that implementing a CBT approach to ART adherence treatment and intervention can lead to increased adherence rates for this population.

Future Research

Replication of the current statistical methodology with a longitudinal research design would provide greater credence for a prediction model of ART adherence outcomes. A notable limitation of the current study is the use of a cross-sectional dataset, which prohibits causal inference among variables studied. Future research is therefore encouraged to investigate the predictors of ART adherence behaviors for YAAM behaviorally-infected with HIV within a longitudinal design to better understand the cause and effect relationship between psychosocial attributes and ART adherence outcomes. Prominent findings in the current study underscore the value of psychological functioning, recreational substance use, and self-efficacy for accurately classifying patients' ART adherence outcomes. However, these findings do not expound the underlying mechanisms that explain how such attributes influence ART adherence behaviors.

In addition, the current study found that the constellation of global mental health distress and weekly cannabis use was the most salient combination of predictors associated with ART non-adherence. It is imperative to identify if this amalgamation of variables are truly more predictive than other related factors (e.g., depressive symptoms and alcohol use), or if a constellation of other mental health and substance use factors may also be as accurate predictors for those at greater risk. If not, elucidating the unique

factors associated with global mental health distress and cannabis use with respect to ART non-adherence will be important to ascertain, in order to create better targeted adherence interventions. Therefore, it will be imperative that future research continue to expound the underlying mechanisms of the aforementioned variables with regard to ART adherence behaviors.

The present study also presents the opportunity for primary care providers to more accurately predict ART adherence outcomes by understanding patients' mental health, substance use, and self-efficacy profiles. However, future research focused on evaluating the specific psychosocial measures or tools that can be used most effectively in primary care settings to predict ART adherence among specific patient populations is necessary. Specifically, the development of a standardized psychosocial assessment battery that provides a risk profile for ART non-adherence would have great clinical utility. Thus, in order to do so, future research should evaluate which mental health and substance use instruments are best able to identify patients who are likely to be ART non-adherent and able to be utilized in time-limited clinical settings.

Strengths

This study has several notable strengths that should be highlighted. First, this research is among the first study to exclusively investigate the predictors and pathways towards ART adherence outcomes among a large multi-site sample of YAAM behaviorally infected with HIV. This is noteworthy, as this population is at increased risk for new HIV infections and has evidenced poor ART adherence behaviors once starting such treatment protocols. Second, this study employed an innovative statistical technique

(ODA) that maximizes the classification accuracy for predicting ART adherence outcomes. Moreover, the use of ODA allowed for the inclusion of a large number of theoretically justifiable variables in one statistical model without increasing statistical error. This analysis allowed for a greater understanding of how predictors interact to ultimately influence ART adherence outcomes. In addition, this analysis allowed for the identification of the specific predictors that were most important for different subpopulations among YAAM behaviorally-infected with HIV (e.g., participants with low psychological distress vs. high psychological distress). Thirdly, the results presented are parsimonious, easily understood, and can be applied to clinical and intervention settings. Furthermore, this study identifies contexts of increased risk (for ART non-adherence), contexts that may buffer against ART non-adherence, as well as highlights factors or areas that future intervention/prevention programs would benefit from including in their efforts to increase ART adherence. As such, the results can help clinical providers identify patients who are in need of greater ART adherence intervention, as well as the likely benefit of adjusting patient care models to include a strong psychosocial component. Lastly, the results from the present study advance the scientific study of ART adherence for a population disproportionately afflicted at higher rates by the HIV pandemic than other populations, but which has been understudied by the greater scientific community.

Limitations

Several limitations in this study should be noted. First and foremost, the use of a cross-sectional dataset does not allow for a causal prediction model to be substantiated.

Secondly, in the current study, a number of constructs of interest were limited by ceiling effects (i.e., physician-patient relationship variables) or not being as broad of a measurement (i.e., social support) as desired. In addition, some constructs of interest to the current study, such as neurocognitive functioning, stigma and discrimination, and decisional balance were not available in the dataset utilized. Thirdly, the dependent variable of complete adherence was based on participant self-report over a seven day period. Although, self-report has been established as a reliable and valid measure of ART adherence (Simoni et al., 2006), it is susceptible to response-bias and a multi-method assessment approach of adherence (i.e., self-report with pill monitoring devices) or a direct measure of viral load would be ideal. Furthermore, the duration of seven days may be too short to classify individuals as being ART adherent or non-adherent. However, prior research has indicated that such a duration is easily recalled by participants and is likely to produce a more valid recall of adherent behaviors than having participants recall longer periods of time (i.e., a 30 day time period). Given that a seven day recall period was used in the present study, ART adherence was defined as taking 100% of all doses prescribed, which is ideal, but slightly above and beyond what is necessary for optimal viral load suppression (i.e., needing to take 90-95% of doses prescribed; Davies et al., 2006; Paterson et al., 2000; Wutoh et al., 2003). In addition, all independent variables were obtained via self-report and are also susceptive to response biases. The generalizability of this study may be limited beyond YAAM behaviorally infected with HIV. Future research is therefore encouraged to explore the attributes that may be most accurate in classifying ART adherence behaviors in other populations afflicted by

HIV/AIDS. In addition, although the age range of participants in the current sample included individuals between the ages of 12-24 years-old, the vast majority of participants were between the ages of 18-24 years of age. Thus, the generalizability for YAAM under the age of 18 is somewhat limited as well.

Conclusion

This study represents one of the first attempts to identify the most accurate predictors and profiles of ART adherence outcomes for YAAM behaviorally-infected with HIV from a large nationwide multi-site sample. The use of ODA allowed for a deeper understanding of how attributes interact to influence ART adherence behaviors and identified subpopulations of YAAM behaviorally-infected with HIV who are at reduced risk for ART non-adherence, as well as those who are at greater risk. Overall, findings from the current study highlight the strong influence of substance use, psychological functioning, and self-efficacy for medical care with regard to ART adherence outcomes. Attributes related to frequency of substance use and the likelihood of current substance abuse issues were the single best predictors of adherence outcomes among all attributes in the current study.

The prediction accuracy for ART adherence outcomes was greatly increased when profiles combined both mental health and substance use attributes. Specifically, for YAAM behaviorally-infected with HIV, this study identified that the greatest likelihood for ART adherence was among those who reported lower levels of psychological symptoms and an absence of current alcohol use. In contrast, the group of participants with the greatest likelihood of being ART non-adherent was those who reported higher

numbers of psychological symptoms and engaged in weekly cannabis use. Furthermore, this study identified the potential protective function of self-efficacy for medical care engagement with regard to ART adherence behaviors. For participants who have higher levels of psychological distress, increasing self-efficacy for medical care engagement is associated with the greater likelihood of ART adherence. The current study thus indicates that multiple pathways toward adherence behaviors exist and that there are several target areas for intervention. However, this study also identified that this protective function may have some limitations, as this finding was moderated by level of current cannabis use. Lastly, alcohol use was found to be a noteworthy risk factor for ART non-adherence, even among those with low levels of psychological distress.

This study provides a strong empirical basis for including psychosocial factors as focal points of HIV treatment and interventions. Although, the prior literature stresses the notable influence of depression and anxiety with regard to ART adherence behaviors, the current study identified that global psychological distress may be just as, or more important than focusing on internalizing distress alone. Thus, an emphasis by treatment providers and interventionists for the overall mental health functioning across psychological and emotional domains is likely critical for improving ART adherence outcomes among YAAM behaviorally-infected with HIV. In addition, given the high comorbidity of HIV and recreational substance use (i.e., tobacco, alcohol, and cannabis) and the negative impact of such use for adherence outcomes, treatment settings are implored to incorporate substance use education and treatment programming as part of routine patient care.

In conclusion, the medical needs of YAAM behaviorally-infected with HIV are likely to be best met within integrated primary care treatment teams, consisting of multidisciplinary professionals focused on both the psychosocial and medical needs of this population. Scholars have voiced the need for multifaceted, interdisciplinary, and integrated health services for individuals living with HIV with a focus on adherence, substance use, and mental health (Altice, Kamarulzaman, Soriano, Schechter, & Friedland, 2010). It is recommended that the unique developmental and cultural needs of YAAM behaviorally-infected with HIV be well understood by treatment providers and incorporated into treatment settings and interventions targeted at this population. Fortunately, evidence-based treatments for the aforementioned issues already exist and behavioral interventions with a strong focus on CBT principles, psychoeducation, and problem solving techniques that have already been shown to be effective among individuals living with HIV- including those with comorbid substance use and/or mental health needs (Daughters et al., 2010; Parsons et al., 2007; Safren et al., 2009) can be utilized in order to best serve this population.

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VITA

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While at Loyola University Chicago, Dr. Gross severed as the chair for the employment committee, and was Vice-President of the Social Committee. In addition, he served as the chair for the Student Advisory Committee. Dr. Gross was the recipient of several honors and awards during his tenure at Loyola. He was awarded a multi-year National Research Service Award from the National Institute of Health and a Child and Family Research Assistantship Award for Loyola University Chicago.

Dr. Gross successfully completed his internship training at the University of Chicago Medical Center in the Pediatric Neuropsychology/Child Psychology program. Dr. Gross will be completing a Clinical Neuropsychology Fellowship at Stroger Hospital of Cook County in Chicago, IL, as well as continue his research examining pathways of medication adherence among youth living with HIV/AIDS.