Factors related to medication adherence and viral variability in HIV+ individuals

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Shannon R. Bierma
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Dedication

To the gay community, for trusting me and letting me see into a world where true strength exists.

To Mo, for inspiring me.

And to Jim, for forever changing my life.

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Abstract

Research on HIV treatment has indicated there are numerous factors that contribute to medication nonadherence, and therefore, risk of transmission. Mental health issues, substance abuse, and co-occurring physical health issues have shown to have negative impacts on HIV medication adherence. Additionally, living in a rural area compared to an urban region negatively impacts adherence. African American males fare the worst in HIV treatment, having the least engagement with HIV care resulting in late stage HIV upon diagnosis, and are within a group that are at the highest risk of infection. Gender role socialization theory and research on male help-seeking behavior guides the current study that aims to investigate predictive factors and the intersection of these factors on HIV medication adherence. This theory states that males are less likely to seek medical and mental health care, or underreport symptoms. Participants were 133 Ryan White Part B clients who have received support and treatment for HIV for at least two years. A retrospective longitudinal design examined how intersecting factors predicted viral variability and CD4 counts in HIV-positive (HIV+) individuals. It was hypothesized that mental health issues, substance abuse, physical health comorbidities, region (e.g., South versus North), and race (e.g., African American/Black versus White counterparts) would impact viral variability and CD4 counts. Results showed that substance abuse, changes in urban/rural residence, and physical health comorbidities impacted viral variability or CD4 counts, and ultimately, substance abuse had the greatest negative impact. Implications of these findings can guide future research and clinical interventions for co-treating substance abuse and HIV.

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Chapter 1

Introduction

Human Immunodeficiency Virus (HIV) is one of the largest epidemics and most difficult to mitigate in the United States (US) and world. HIV can lead to Acquired Immune Deficiency Syndrome (AIDS), which is often fatal. According to the Centers for Disease Control (CDC) it is estimated that around 1.1 million people live with HIV in the US currently, and approximately 15% of those are unaware of being infected. Though HIV infection rates have steadily declined in some groups since the mid-1990s (injection drug users, heterosexual men and women), other groups have experienced increases in infection rates during recent times. Gay and bisexual men are most impacted by HIV, and they account for 82% of all diagnoses among males, and 67% of diagnoses overall. Black/African American gay and bisexual men account for the largest number of HIV diagnoses, closely followed by their white counterparts (CDC, 2018). Though overall HIV infection rates suggest a decline in new infections, the progress has been imbalanced.

According to the most recent data collected by the CDC, an estimated 39,513 new infections were reported in 2015. Of these diagnoses 26,376 were gay and bisexual men, 10,315 of which were Black/African American. From 2010 to 2014, trends have varied by race for HIV infections. Diagnoses decreased in all groups with the exception of Black/African American males, who experienced a 2% increase. Approximately 8,600 HIV infections in 2015 were among straight-identified individuals, and 2,800 among injection drug users (IDUs). HIV diagnoses are also not distributed evenly among geographic regions. Rates of people who receive an HIV diagnosis (per 100,000 people)

were highest in the South (16.8), followed by Northeast (11.6), West (9.8), and Midwest (7.6) (CDC). In 2015, 18,303 people were diagnosed with AIDS, adding to the total since the epidemic arose in the early 1980s of 1,216,917 people (CDC).

HIV infection rates in the South are unique, and do not reflect those of most national reports. Southern states (Texas, Oklahoma, Arkansas, Louisiana, Mississippi, Alabama, Tennessee, Kentucky, Georgia, South Carolina, North Carolina, Florida, Virginia, West Virginia) account for almost 44% of individuals living with an HIV diagnosis in the US, which is higher than all other regions (CDC). The South faces geographical disparities where most of the HIV diagnoses occur in urban areas; however, there are higher rates in suburban and rural areas in comparison to regions nationwide. Because many people living with HIV in the South do not receive treatment, mortality rates are startlingly high – with death rates three times higher than other states. The South accounted for nearly half of all deaths reported from complications of HIV infection in 2013 (CDC). Poverty and poorer health outcomes have historically been widespread in southern states and, along with high numbers of people without health insurance, contribute to the high rates of HIV infection in the South. Furthermore, cultural factors such as homophobia, transphobia, racism, and religious oppression of sexuality may have created an overall discomfort with discussions about sexuality in the South. These factors can produce higher levels of stigma, which in turn, may limit people's readiness to seek out HIV testing, treatment, or prevention support. Since the HIV rates in the South are disproportionately high, it is critical to investigate factors related to medication compliance in HIV+ individuals in the region so efforts can be made to avert such factors that obstruct an individual's desire to participate in and adhere to treatment. Research on

HIV in the South has examined predictive factors to medication adherence, which primarily includes mental health and substance use issues, physical health comorbidities, region, and ethnic background. The following will offer a brief history of HIV, treatment discoveries, and theoretical considerations regarding medication adherence, as well as supportive literature on the correlates of these factors and medication adherence. Finally, the rationale for this study's focus will be provided, illuminating the importance of assessing these factors concurrently and longitudinally.

Definition, History and Treatment

Human Immunodeficiency Virus, or HIV, weakens immune function by destroying white blood cells that fight infection and disease (CDC, 2018). It is a virus that is spread through bodily fluids and attacks CD4 cells (T-cells). Untreated, the virus can destroy enough T-cells that the body is no longer able to fight infection or disease, such as opportunistic cancers (CDC, 2018). Infections or cancers can take advantage of the weakened immune system and signal that the body has Acquired Immune Deficiency Syndrome (AIDS). This final stage of HIV infection renders the body so damaged that it cannot defend itself any longer. The progression rate of HIV varies with overall health, age, and background of the individual. Though no cure exists, HIV can be controlled with highly active antiretroviral therapy (HAART). When HAART is taken properly the viral load can lower to a level that is undetectable in the blood, which also presents no risk of further transmitting the virus. Individuals with suppressed viral loads are able to live long and extended lives – similar to those who do not have HIV.

HIV is traced back as early as 1931, where it was discovered in a blood sample of an individual in the Democratic Republic of Congo (CDC, 2016). It is

theorized that the virus was spread from chimpanzees, when hunters would come in contact with the animal blood. The earliest case in the US was confirmed in 1968, in a 16-year-old male from the Midwest who had never left the region, nor received a blood transfusion. It is suggested that the virus may have been present in the US prior to 1966. The epidemic of HIV beginning in 1981 was originally believed by the medical community to spread via blood transfusion, men who have sex with men (MSM), and injection drug users (IDUs). It was discovered that these routes of transmission were valid, but it was later found that women could also get HIV by sexual transmission (CDC, 2015). Throughout the 80s and 90s, research, funding, and treatment facilities propagated as the virus spread exponentially and quickly became the leading cause of death for adults aged 25 to 44 years (CDC, 2016). By 1995, around 50,000 Americans had died from AIDS related causes, 49% of which were African American. HAART became widely available in 1996, and since then, the number of related deaths have dropped by over half over 15 years (CDC, 2016).

HAART has provided even more dramatic reductions in mortality and morbidity from HIV infection (Murphy, 2001). HAART has shown significant evidence in improving CD4 cell counts, a type of white blood cell that protects the body from infection, along with generating viral suppression (or virologic control) where the HIV RNA (ribonucleic acid) is undetectable (Walensky et al., 2006). The first drug available, Saquinavir®, was a protease inhibitor that targeted the protein needed for HIV to replicate itself. This was used in combination with other nucleoside analogue medications, which began the age of combination therapy for HIV (CDC). By the early 2000s, single tablet medications were developed and approved (with both protease inhibitors and nucleoside

analogues), but later identified as having metabolic toxicities and abnormal body fat changes. Other drugs during this time were found to cause bone and kidney issues, so numerous trials were initiated by several drug companies. By 2004, Truvada® was approved, which is commonly used today. U.S. guidelines about starting HAART fluctuated throughout the first decade of the 2000s, ranging in CD4 counts of 350-500 (CDC). Around 2014, the newest generation of medications was approved and consists of once or twice daily doses that have not been found to have as many negative side effects. Truvada® is now also used as a pre-exposure prophylaxis (PrEP), which prevents HIV transmission to non-infected individuals. During viral suppression, HIV still remains in the body but the copies per milliliter within the blood are low enough that the likelihood of spreading the infection is almost none (CDC, 2016). Additionally, when an individual with HIV obtains viral suppression, the risk of other health related complications is significantly reduced. Successful long-term management of HIV is thus obtained when infected individuals are connected to medical care early and remain compliant with their medication.

In recent years, medication adherence in HIV+ individuals has gained substantial attention, as it has been recognized by the Department of Health and Human Services as the most effective step in obstructing disease transmission (Department of Health and Human Services [DHHS]). Medication adherence is shown through viral load levels and CD4 counts in individuals who are HIV+. Individuals who adhere to their medication regime have lower viral loads, and can maintain them at a level where they are undetectable and therefore, untransmittable. Variations in viral loads and CD4 counts express that the individual is not taking their medication consistently, allowing the virus

to duplicate and negatively impacting their immune response, which is reflected in lowered CD4 counts. Despite recognizing the importance of adherence, there is minimal research that investigates the intersection of factors that can negatively impact medication adherence in HIV+ individuals (Buchanan et al., 2012; Belenky et al., 2013; Panos et al., 2014; Tyer-Viola et al., 2012), especially unique factors of those who reside in the South (Konkle-Parker et al., 2012; Phillips, 2007). HAART became widely available and HIV began to be considered a manageable chronic disease, so research into barriers to care and medication adherence did not gain focus until specific populations of individuals experienced increases in infection rates over the last ten years, such as those in the African American and gay communities. It remains essential to further examine medication that reduces viral load and thus, reduces risk of transmission. However, it is equally essential to study those factors that influence medication adherence, including metal health and substance use issues, physical comorbidities, regional access, and ethnic background, each of which will be discussed below.

Theoretical Framework

While considering all of the following factors that have been shown to negatively impact medication adherence in HIV+ individuals, there may be larger theoretical explanations to help understand issues with HIV treatment compliance. Research shows that men are less likely to seek out health services compared to women (Vogel et al., 2011). This is problematic, given that men are at higher risk for substance abuse problems in general, and more specifically, within the HIV risk population. Furthermore, men of non-majority backgrounds seek out help less frequently than other groups of men (Chandra et al., 2009). Conversely, straight-identified men are less likely

to seek help compared to gay-identified men (Cochran et al., 2003). Though research has demonstrated that help seeking disparities exist between men and women, our understanding of why such differences are present is limited.

Addis and Mahalik (2003) researched male help seeking behaviors and found that men did not seek necessary medical care, ask questions of their providers, follow health advice, or attend medical appointments. African American males, especially, have low rates of health care use or screening opportunities (Griffith et al., 2007). Even more troublesome, men often delay seeking medical care until their symptoms considerably affect their daily functioning (Ravenell et al., 2008). There are numerous reasons why men tend to delay or avoid seeking medical care. For example, men generally have less favorable attitudes toward seeking or receiving help compared to women. Masculine norms in US culture dictates that men should be self-sufficient and controlled, which is inconsistent with help seeking (Mahalik et al., 2003). Based on Good's (1989) research on gender role conflict (GRC), Addis and Mahalik (2003) attempted to identify how masculine ideologies can have negative consequences on men's well-being under the masculine gender-role socialization paradigm. This theory states that men's internalization of ideas that they should be "tough" and "unemotional" can have serious negative effects on their mental and physical health. Furthermore, it considers how men endorse cultural norms and values regarding gender roles and the impact that can have, which could be more ambiguous in the men who have sex with men (MSM) population in this study. Struggling with one's gender role could also be an underlying precipitant to mental health struggles, substance abuse, and even physical health. Understanding how

gender role socialization influences men's help seeking can further guide future interventions and barriers to care.

Public stigma toward HIV, related to the previously mentioned "toughness" of gender role socialization, may have a significant negative impact on men's help seeking behaviors as well. Research suggests that men internalize, or make part of one's nature, public stigma more than women; that is, they internalize help seeking behavior as weak or inferior traits that are undesirable (Vogel et al., 2007). Identifying factors that mediate male gender norms and help seeking behaviors is important, especially within the HIV+ population. Stigma appears to be the central obstacle to help seeking, in both public and internalized realms (Magovcevic & Addis, 2005; Vogel et al., 2007, 2009, 2011). Considering that stigma influences help seeking behavior in men may further explain medication nonadherence in the current study.

Other theories are often used in this area of research, such as Theory of Planned Behavior (TPB), and the Health Belief Model (HBM). TPB suggests that medication adherence is determined by one's perceived behavior control (Ajzen, 1985). This is often assessed through measures such as the Medication Adherence Rating Scale (MARS), and the Medication Adherence Self-Efficacy Scale (MASES). Since these data did not include either of these measures, it was not possible to assess each individual's perception of medication adherence. The HBM is descriptive and looks at individual's perceived susceptibility and severity of disease, along with the benefits and barriers of adhering to medication (Rosenstock, 1960). This framework does not account for habitual behavior, social stigma, or environmental/economic factors that relate to

medication adherence. For these reasons that are related to the individuals assessed in this study, it also could not be applied.

Mental Health and Substance Abuse

Patients with HIV often have co-occurring mental and substance use disorders, which are associated with negative outcomes such as poor adherence to HAART medication and reduced quality of life (Kaaya et al., 2013). Rates of mental and substance use disorders in HIV-positive (HIV+) individuals exceed those of physical health co-morbidities (Goulet et al., 2007), though these factors will be explored next. Yehia et al (2015) found that over two years of monitoring HIV+ patients in an urban location, around half (49%) had a diagnosed mental illness. Of these individuals with mental illness, there was less viral suppression compared to those who did not have mental illness (65.9/74.4). HIV+ individuals who were symptomatic were also twice as likely to experience clinical depression compared to those who are not infected (Owe-Larsson et al., 2009).

Factors such as stress of managing the infection, stigma, negative neurological effects of the infection, housing and food insecurity, and other environmental factors, can exacerbate mental health disorders. In a study investigating the effects of depression on medication adherence, Belenky et al (2012) found that depressive symptoms correlated highly with reported medication nonadherence over 12 months. Furthermore, they found that increases in depressive symptoms were also associated with lower CD4 counts. Another study found that anxiety symptoms were highly associated with medication nonadherence among HIV+ individuals who received mental health care (Schonnesson et al., 2007). Related, other clinical trials have found

improvement of medication adherence when anxiety symptoms are also treated (Cook et al., 2006; Safren et al., 2009; Yun et al., 2005). Studies investigating high pathology and psychiatric patients who live with HIV yielded findings that suggested that psychotropic medications with noticeable effects, such as those that have sedating properties, took priority over HAART primarily because of the immediate and obvious side-effects of not adhering to it (Kalichman et al., 2015; Moore et al., 2012).

Additionally, alcohol and other substance abuse is common in HIV+ individuals receiving treatment, with estimates up 56% and is especially high in aging patients whose viral load has never reached suppression due to suboptimal medication adherence (Jaquet et al., 2010). Substance use, across all studies, is one of the most constant barriers to HIV medication adherence. Several studies suggest that food and housing insecurity, a common obstacle for HIV+ individuals, is also strongly associated with higher likelihoods of substance dependence, thus fueling this cycle (Duncan et al., 2014; Surratt et al., 2014). Furthermore, coping and self-regulation theories of substance abuse imply that substance use behaviors may be engaged when one believes it will help them cope with their adverse life events and stress, which often are accompanied with HIV diagnoses and treatment (Gonzalez et al., 2011). Differences among substance use and HIV medication adherence suggest that poly-substance users have the most difficulty adhering to medication (Parsons et al., 2014). Still, individuals who use alcohol, methamphetamines, or other substances exclusively, also produce troubling findings in HIV treatment research. For example, Pellowski et al. (2016) found that reported days of alcohol use could predict daily missed doses of HIV medication. Further studies of alcohol consumption and HIV medication nonadherence also found that individuals

missed more doses of medication and were less likely to reach viral suppression when they drank alcohol often (Kalichman et al., 2014). Methampetamine use, a considerable risk factor for HIV infection in gay men, also contributes to the progression of HIV by damaging the immune system and increasing viral loads, and by decreasing daily medication adherence by 2.3 times (Moore et al., 2012; Parsons et al., 2013). Because of the vast research showing how mental and substance abuse issues impact medication adherence in HIV+ individuals, it seems reasonable to expect that mental health and substance abuse will have negative effects on medication adherence in this sample as well.

Physical Health

Just as obstacles of mental and substance abuse issues contribute to HIV medication nonadherence, other chronic medical conditions have a negative impact on adherence as well. It is reported that approximately 90% of individuals who are HIV+ have at least one comorbid condition, with hypertension, kidney failure, heart disease, and high cholesterol being the most common (Duchane et al., 2013). Because people are living longer with HAART available, chronic medical comorbidities are becoming more common. Among individuals who are HIV+ and over the age of 50, it is usual to have at least four comorbidities, which increases the likelihood of taking more than five medications daily (Monroe et al., 2013). This can worsen HIV medication adherence, as complexities of polypharmacological regimens can lead to unwanted side effects or even "pill fatigue." Several studies about HIV comorbidities reveal a common theme: that sufferers are often more concerned with pressing health issues that have greater negative consequences compared to those of HIV (Gao et al., 2010; Krentz et al., 2012).

Anecdotal information from participants in these studies expressed concerns about heart attack, stroke, limb amputation, and frustrations surrounding the lack of control over certain conditions (i.e., blood pressure). These concerns took precedence over HIV medication anxieties, as HIV medication noncompliance did not have as immediate of consequences or mortality risk. This literature further suggests that other complicating medical conditions, similar to mental and substance abuse disorders, will negatively impact one's HIV medication adherence.

Regional Considerations

There are significant disparities in health care access and utilization of such in rural communities, especially in the South. Numerous contextual factors contribute to the barriers of care in these communities, including stigma related to HIV, conservative worldviews, discrimination, lack of transportation, and a lack of health care service overall (CDC, 2016; Reif et al., 2011; Sutton et al., 2010). Studies in the US reveal that rural HIV+ individuals are much more likely to be diagnosed at late stage infection compared to their urban counterparts (Ohl et al., 2011). This could suggest that rural areas do not have as many opportunities to be tested for HIV, and therefore, individuals go undiagnosed and untreated for longer. In nationwide analyses of medical service use for HIV, results found that rural individuals who were HIV+ were less likely to have four or more outpatient doctor visits (as suggested by the Department of Health) compared to their urban counterparts (Wilson et al., 2011). Costelloe et al. (2015) also found higher depression scores in rural HIV+ patients, which predicted perceived stigma of the disease and treatment – further supporting the aforementioned.

HIV+ individuals in Tennessee are a unique population. Though they share similarities with national samples of HIV+ individuals, their demographics are slightly different than their fellow Southern equivalents. In the South, there is almost a 3:1 infection rate of young, African American/Black MSM males compared to their White counterparts (CDC), yet the primary group who receives treatment in Tennessee is White MSM. Additionally, there are higher rates of straight, Black females becoming infected as well for reasons that are not yet understood. The difference in Tennessee, compared to other Southern regions, is that efforts to reach rural regions and the target demographic have only recently begun. There is a high likelihood that the state reported HIV infections are inaccurate because of barriers to rural outreach and linkage to care. East Tennessee, being in the foothills of Appalachia, has few urban regions and vast amounts of rural seclusion. Though the urban regions provide adequate prevention testing and care for HIV+ individuals, the reach into rural areas has been marginal. Having minimal access to HIV testing, high rates of IDUs, stigma, and isolation, are all factors that exacerbate the HIV transmission in East Tennessee. Exploring barriers to treatment in this region could help steer future efforts to combat the epidemic that is plaguing this area.

Race and Ethnic Factors

As previously mentioned, African American/Black males are disproportionately infected with HIV in the US (CDC, 2016). They represent almost half of all males diagnosed and have the highest rate of diagnoses among all racial groups, with even higher rates within MSM. HIV+ African American males exhibit worse medication adherence and poorer health outcomes compared to their White and Latino counterparts (Simoni et al., 2012). Explanations of this health disparity closely resemble

those of rural populations such as poverty, low testing rates, minimal access to health care, stigma, unstable housing, and homophobia (Abbot et al., 2015; Gray et al., 2016; Webel et al., 2014). Some of this is due to the high prevalence of African Americans living in rural communities in the South, which is especially detrimental to health outcomes. Because of these inequities, African Americans living in the South are less likely to be insured, less likely to have access to medical and mental health care, are more likely to have substance abuse issues, and are more likely to have other chronic health conditions (Stephens et al., 2014).

Medical distrust has been shown to be especially high in African Americas/Blacks, possibly linked to prior experiences with racism or discrimination by health care providers (Hausmann et al., 2013). This mistrust of medical providers has also been related to unwillingness to partake in health screenings, such as those for HIV (Davis et al., 2012). This research further suggests that African American males would have poorer health outcomes, and less medication adherence. Additionally, exploitation of minority populations in medical research, such as those in the Tuskegee Syphilis Study, have been cited as obstacles to participation in medical treatment by ethnic minorities (Shavers, et al., 2002). Though factors related to this disparity of health are beginning to be understood, focusing attention toward this group would be beneficial so means to promote positive health outcomes for African American males can be expedited.

One of the most thorough longitudinal studies investigating factors that impact medication adherence in HIV+ individuals found that all of the aforementioned factors are predictive for medication nonadherence (Panos et al., 2014). This study assessed

compliance over time through pill bottle electronic monitoring devices. They assessed medication side effects, drug use, self-efficacy, and psychiatric factors and found that drug use and mental illness were predictive factors, but there was great variability in medication adherence over time. Although multiple factors were assessed, there are limitations in this study. First, medication adherence was measured through the opening of a pill bottle and not biological data. This cannot determine medication adherence accurately, as participants could have opened the bottles and not taken their medication. Also, the study only monitored participants for six months, which limits the predictive capacity of the information. Other longitudinal studies of medication adherence in HIV+ individuals suggest that the previously mentioned factors may predict medication adherence, but are limited by self-report measures (Buchanan et al., 2012), are not in the US (Belenky et al., 2013), or are exclusively about women (Tyer-Viola et al., 2012). Previous research limits the ability to make predictive generalizations about this population, therefore this study would be one of few to investigate long-term longitudinally how combined factors impact medication adherence in HIV+ individuals utilizing biological data as a variable. For this study, a local facility that serves individuals with HIV was utilized to better understand medication adherence in this region.

Positively Living is a non-profit organization in Knoxville, Tennessee that began as a support facility for those living with HIV in 1997. It evolved in 2003 to a housing facility for these individuals; offering housing support, medication support, and food vouchers through the Ryan White Part B program, fully becoming a social services program in 2012. Positively Living grew extensively over time, now encompassing a

primary care treatment facility (Choice Health Network), an HIV prevention program (Project ACT), mental health services, and syringe exchange. This facility serves as a reliable historical picture of how HIV has impacted a region, with no prior research on their client population.

Present Study

Previous research suggests there are numerous factors that contribute to medication nonadherence in HIV+ individuals. There have been few studies assessing longitudinal data of HIV treatment that examine predictive factors for medication adherence (Buchanan et al., 2012; Panos et al., 2014). There are few studies that assess multiple factors over time and how they interact with one another, which is critical in understanding the intersection or isolation of such factors in medication nonadherence. These studies are limited by self-report measures and experimental conditions, but do not utilize biological data (Buchanan et al., 2012; Panos et al., 2014). Gender role socialization theory suggests that men are at higher risk of mental and physical health issues because of their lack of help seeking. Therefore, there is a high likelihood that intersecting factors of mental health, substance abuse, physical comorbidities, region, ethnic background, and gender will impact one's HIV medication adherence since this population is primarily male. The broad aim of this retrospective longitudinal study is to assess how these factors intersect and may predict medication nonadherence, expressed in viral load and CD4 levels. Since there is research suggesting that these factors impact medication adherence individually, it could be expected that assessments of these factors individually would mirror that of previous research. Concurrent and longitudinal assessments of these factors will provide additional information about how they influence

medication adherence over time and how each factor may intersect with other factors. Based on previous research, it is likely that a combination of risk factors will best predict medication nonadherence. Additionally, cross-sectional associations of factors may be predictive of medication adherence, which will be illuminated through the longitudinal design. Furthermore, the largest demographic receiving treatments for HIV in this sample are MSM, who have shown fewer help seeking behaviors historically. This knowledge could serve to improve biopsychosocial approaches to HIV treatment for this particularly at-risk group, and eliminating barriers to treatment by addressing all facets that negatively impact medication adherence.

Based on previous research and gender role theory, it can be assumed that gender norms and behaviors related to help seeking, coping, and stressors would drive the following results. Therefore, the primary hypotheses are as follows:

1. Over a 2-year period, individuals with a history of mental illness will experience higher incidents of medication non-compliance, reflected in greater means and variability in viral loads and suboptimal CD4 counts compared to those who do not report a history of mental illness.

2. Over a 2-year period, individuals with substance abuse issues will experience higher incidents of medication non-compliance, reflected in greater means and variability in viral loads and suboptimal CD4 counts compared to those who do not report substance abuse issues.

3. Over a 2-year period, individuals with negative physical health conditions will experience higher incidents of medication non-compliance, reflected in greater

means and variability in viral loads and suboptimal CD4 counts compared to those who do not report physical health conditions.

4. Over a 2-year period, individuals from rural areas would experience higher incidents of medication non-compliance, reflected in greater means and variability in viral loads and suboptimal CD4 counts compared to their urban counterparts.

5. Over a 2-year period, African American individuals would experience higher incidents of medication non-compliance, reflected in greater means and variability in viral loads and suboptimal CD4 counts compared to their counterparts.

Exploratory hypotheses

One of the major goals of this study is to examine the intersectionality of these factors. However, there is limited theoretical basis for predicting which factor(s) would uniquely predict medication adherence, while controlling for other factors, and/or which factors would interact to predict medication adherence. The literature suggests that being African American may emerge as the strongest predictor of medication adherence, but this may occur through the mediating role of other factors. This study will explore:

6. The extent to which each factor uniquely predicts medication adherence over 2 years when controlling for all other factors, and

7. Because this is a possibility, this study will explore the potential mediating effects of mental illness, substance use, physical health, and region on the relationship between race and medication adherence.

Chapter 2

Methods

Participants

Version 3.1.9.3 of G* power (Henrich & Heine, 2014) was utilized to calculate the required sample size to assess the primary hypotheses in the current study. A one-way ANOVA design with a significance value of .05 and a power level of $(1 - \beta) = .80$ was used, and the required sample size for exploring medium to large differences was quantified. A medium effect size is shown to be equal to .25, with a large effect equal to .40 (Cohen, 1988). Computations showed that sample sizes ranging from 26 participants (effect size = .25) to 64 participants (effect size = .40) were needed.

In the current study, participants were 133 clients who received services for at least 2 years from the Ryan White Part B program at Positively Living from 2012-2018. De-identified client files were utilized to gather retrospective data on the participants. The sample was at least 18 years of age, predominantly male (N = 101, or 76%), with one Transgender participant (male to female or M to F). The mean age of the sample was 46.5 years old (range = 22-68 years old, SD = 11.32). Ethnically, clients identified as mostly White, non-Latino (63%) or African American (31%). The remainder of the clients identified as Latino (5%) or Native American (1%). Clients were diagnosed with HIV between 1982 and 2017 (see Figure 1). Transmission of HIV was reported from same-sex contact (N = 72); different-sex contact (N = 43); unknown method (N = 13); IV drug use (N = 2); tattoo (N = 2); and dental work (N = 1). More than half of the clients resided within the city of Knoxville (n=72), while 45 reported living outside of the city in rural zip codes, and 16 reported moving between the city of Knoxville and rural regions.

Educationally, clients reported the following: having less than a high school degree (N = 16); high school degree (N = 54); some college or associates degree (N = 37); bachelor's degree (N = 4); graduate level degree (N = 4); and 18 were unknown.

Measures

Baseline intake files provided information about the participants, including demographic information (i.e., age, location, and race; barriers to medical care, HIV medication and other health medications and conditions), date of HIV diagnosis, HIV transmission category, viral loads, CD4 counts, chronic medical conditions, mental health history, alcohol and drug abuse history, and sexual history.

For each participant, their self-reported chronic medical conditions and mental health conditions were reviewed and grouped by organ system or disease to reduce the number of possible health conditions to be examined. For instance, clients that report hypertension, high blood pressure, heart attacks, and/or abnormal heartbeats were all grouped into "history of heart conditions." Overall, 14 health conditions were identified, which included: self-reported chronic health issues, chronic pain, hepatitis past or present, heart condition, pulmonary condition, vascular issues, eye issues, hepatitis C, kidney issues, liver issues, diabetes, gastrointestinal issues, and auto-immune disease. Mental health conditions that were recorded in participant records included: memory issues past or present, attention-deficit/hyperactivity disorder (ADHD) or attention deficit disorder (ADD), anxiety, bi-polar disorder, depression, panic attacks, psychosis/schizophrenia, post-traumatic stress disorder (PTSD), stress, and history of mental health treatment. Next, for each participant, we summed across intake histories to calculate if they had ever reported any of the medical or mental health conditions.

Because medical and mental health histories were recorded at the individual level, it was not possible to discriminate between the intensity or duration of health concerns or whether client's symptoms or issues had subsided. Thus, medical and mental health data were split into two variables; participants either reported condition in their medical history or they did not.

Next, intake histories were summed to calculate if each participant had ever reported abusing alcohol, using drugs, using intravenous drugs, and whether the client had ever sought treatment for substance abuse. If at any point in a client's medical history they had reported yes for any alcohol, drug, or substance abuse treatment, the client was deemed to have a history of alcohol, drug, or substance abuse treatment within the dataset. Similar to health histories, substance abuse was measured at the individual level which prevented an understanding of the intensity or duration of substance abuse history. To document the stability and location of clients living situation, each client's intake histories was examined for changes in zip codes between visits and whether clients were residing in Knoxville, outside of Knoxville, or transitioning between Knoxville and outside of Knoxville.

Procedure

During 3-month check-ups, clients reported any changes in status including: health issues, medication (for HIV and other conditions), substance abuse problems, mental illness, and changes in housing. Lab reports from the client's primary care provider (PCP) were gathered and filed with the check-up forms.

Data Analytic Method

All statistical analyses were conducted in R version 3.3.2 (R development core team, 2016) and RStudio version 1.0.44 (RStudio, 2016), with packages cited where applicable. The initial goal of this experiment was to conduct a repeated measures analysis to look at medication adherence and the effect on viral loads and CD4 counts through time. However, inconsistent time gaps between check-up appointments and an inconsistent number of total check-ups made the repeated measures analysis un-interpretable. As an alternative to the repeated measures approach, analyses focused on an individual's mean and variance in viral load and CD4 count. This allowed for the maximization of the number of participants that were included within the study.

To test hypotheses 1-4, simple one-way ANOVAs were constructed with log-transformed mean and variation in viral load and CD4 counts with history of mental health issues, substance abuse, physical health ailments, and ethnicity as predictor variables. Using linear models, data were log-transformed to meet the assumptions of normality.

Next, multiple regression models were constructed to explain mean and variance in HIV viral load and CD4 cell counts. Within each of these multiple regression models, several specific mental health and physical health ailments were examined, including history of substance abuse including alcohol, drugs, and intravenous drug usage, as well as a history of treatment for substance abuse. Additionally, several aspects of demographic information about each participant including ethnicity were examined, including year they contracted HIV, where they live, how stable their housing situation was, religiosity, the mode in which they contracted HIV, ability to read and write, and the

language they speak. Initial models were constructed with all possible predictor variables. From these full models, a multi-model inference and model averaging (Grueber *et al.* 2011) was used to determine which variables (mental health, history of substance abuse, physical health, ethnicity) best predicted outcome measures because there could be a number of similar models due to the collinearity among identity facets. To do the model selection, the *dredge* function in the *MuMIn* library was used to fit all possible models and the *model.avg* function to estimate parameter values, errors, and AIC_c-weighted importance for all models within 4 AIC_c units of the 'best' model (Grueber *et al.* 2011). This allowed for testing which predictors variables best-explained mean and variation in viral loads and CD4 counts, and addressed collinearity among factors. *Dredge* also addresses sampling size weightedness in the analyses.

The final averaged multiple regression model was used to parameterize a structural equation model to help better explore the relationships among predictor variables, viral loads, and CD4 counts. Multilevel path analysis (Shipley 2009; 2013) using the *piecewiseSEM* package (Lefcheck, 2017) was conducted with the initial model including all the identity facets that were retained within the final averaged multiple regression models for viral load and CD4 count mean and variance. The 4 regression models were combined within and tested for goodness-of-fit using the d-separation test (Shipley, 2009), derived an AIC score from Fisher's *C* statistic (CIC) (Cardon et al. 2011; Shipley, 2013), and extracted path coefficients from models that fit using the *sem.fit* function. Next, additional paths were fitted, including correlated error terms, and removed non-significant paths from the model based on estimates of path strength using a step-wise fitting procedure. To improve model fit, correlated error terms were added

between pairs of factors. From the best fit model, standardized path coefficients and calculated p-values using F-tests comparing models were reported with and without the path using denominator degrees of freedom using the Kenwood-Roger method (Lefcheck, 2016). Finally, the variation explained by the four regression models (Nakagawa & Schielzeth, 2013) was reported.

Chapter 3

Results

Hypothesis 1. Hypothesis 1 proposed that over a 2-year period, individuals with a history of mental illness will experience higher incidents of medication non-compliance, reflected in greater means and variability in viral loads and CD4 counts compared to those who do not report a history of mental illness. Results indicated that hypothesis 1 was not supported. Specifically, comparisons of viral load means between participants having a history of mental illness (M = 9,447) or not having a history of mental illness (M = 14,143) showed no differences ($F_{(1,131)} = 0.42$, $p = 0.52$), nor did they for viral variability ($F_{(1,131)} = 0.54$, $p = 0.46$). Similar results occurred for CD4 counts for means ($F_{(1,131)} = 0.001$, $p = 0.98$), and variability ($F_{(1,130)} = 0.38$, $p = 0.54$). See Tables 1 and 2 for full viral and CD4 parameters for all hypotheses.

Hypothesis 2. Hypothesis 2 proposed that over a 2-year period, individuals with substance abuse issues will experience higher incidents of medication non-compliance, reflected in greater means and variability in viral loads and CD4 counts compared to those who do not report substance abuse issues. Substance abuse was separated into categories and mean viral loads were reported in alcohol abuse (M = 12,093), drug abuse (M = 15,065), and IV drug abuse (M = 12,014) categories, and compared against individuals who did not report substance abuse with alcohol (M = 8,639), drugs (M = 9,637), or IV drugs (M = 4,468). Results indicated that hypothesis 2 was supported for alcohol abuse, such that viral load means in those who reported alcohol abuse ($F_{(1,131)} = 7.61$, $p = <0.01$) were significantly greater than those without reported abuse. A similar finding emerged for viral variability ($F_{(1,131)} = 6.49$, $p = 0.01$). This

result was further evidenced for drug abuse viral mean ($F_{(1,131)} = 4.41$, $p = 0.04$), but not for viral variability ($F_{(1,131)} = 0.89$, $p = 0.34$). No differences were found for individuals reporting IV drug abuse for mean ($F_{(1,131)} = 0.05$, $p = 0.83$) or variability ($F_{(1,131)} = 0.07$, $p = 0.79$). No differences were found for mean CD4 counts for reported alcohol abuse ($F_{(1,131)} = 3.24$, $p = 0.07$), though there was a trend for viral variability ($F_{(1,130)} = 3.71$, $p = 0.06$) suggesting modestly greater variability for those reporting alcohol abuse compared to those not reporting alcohol abuse. Similarly, no differences were found for CD4 counts for means in individuals who reported drug abuse ($F_{(1,131)} = 2.16$, $p = 0.14$), though a marginal difference was found for variability ($F_{(1,130)} = 3.73$, $p = 0.06$) suggesting modestly greater differences in CD4 variability. No differences were found for CD4 counts for means in individuals who reported IV drug abuse ($F_{(1,131)} = 0.96$, $p = 0.33$)or for variability ($F_{(1,130)} = 0.64$, $p = 0.42$).

Hypothesis 3. Hypothesis 3 proposed that over a 2-year period, individuals with negative physical health conditions will experience higher incidents of medication non-compliance, reflected in greater means and variability in viral loads and CD4 counts compared to those who do not report physical health conditions. Negative health conditions were separated into reported chronic health issues and chronic pain categories, and compared against individuals who did not report chronic health or pain issues. Results indicated that hypothesis 3 was not supported, with the exception of CD4 variability for individuals who reported chronic health issues. Specifically, comparisons of viral load means between participants who reported having chronic health issues ($M = 9,707$), or not having chronic health issues ($M = 13,357$) showed no differences ($F_{(1,131)} = 1.14$, $p = 0.29$), nor did they for variability ($F_{(1,131)} = 1.10$, $p = 0.30$). Comparisons of

viral load means between participants who reported having chronic pain (M = 11,087), or not having chronic pain (M = 11,114) also showed no differences ($F_{(1,131)}$ = 0.46, p = 0.50). No differences were found for viral variability with chronic pain as well ($F_{(1,131)}$ = 0.50, p = 0.48). Similarly, no differences were found for CD4 counts for viral load means with chronic health issues ($F_{(1,131)}$ = 1.52, p = 0.22), however, variability did show differences between these groups ($F_{(1,130)}$ = 4.07, p = 0.05). This suggests that there is greater variability in immune cells in those who also have chronic health conditions compared to those without such health conditions. No differences were found for CD4 means ($F_{(1,131)}$ = 0.04, p = 0.84) or variability ($F_{(1,130)}$ = 0.06, p = 0.80) for individuals who reported chronic pain.

Hypothesis 4. Hypothesis 4 proposed that over a 2-year period, individuals from rural areas would experience higher incidents of medication non-compliance, reflected in greater means and variability in viral loads and CD4 counts compared to their urban counterparts. Results indicated that hypothesis 4 was supported. Comparisons of mean viral loads between individuals who lived in an urban location (M = 5,441), rural location (M = 13,919), or who moved between urban and rural (M = 29,271) showed significant differences ($F_{(2,130)}$ = 5.60, p = <0.01). Additionally, significant differences were found for viral variability ($F_{(2,130)}$ = 3.17, p = 0.05). No differences were found for CD4 means ($F_{(3,129)}$ = 0.07, p = 0.97), however significant differences were found for CD4 variability ($F_{(3,116)}$ = 3.23, p = 0.02).

To understand where the differences occurred between groups, Tukey's post hoc tests were run to determine which groups showed significant differences in means and variability within the log transformed data. Results indicated that living exclusively

in an urban region (*M* = 9.199) compared to living in both rural and urban environments (moving between) predicted higher viral load means (*M* = 15.578; *M difference* = -6.459, *p* = <0.01). Similarly, living in an exclusively rural region (*M* = 8.797) compared to living in both rural and urban (moving between) predicted higher viral loan means (M = 15.578; *M diff* = -6.780, *p* = .01). Individuals who did not move between rural and urban environments showed no differences (*M diff* = -.32, *p* = .97). Variability in viral loads showed similar trends, where living exclusively in an urban region (*M* = 10.123) compared to living in both rural and urban environments (moving between) predicted higher viral variation (*M* = 16.822; *M diff* = -6.70, *p* = .05), as well as living exclusively in a rural environment (*M* = 10.162) compared to living in both rural and urban environments (moving between) trended toward significance (*M diff* = -6.66, *p* = .06). No differences were found in variation for individuals who did not move in between rural and urban (*M diff* = .039, *p* = .99). CD4 means for individuals who lived exclusively in an urban region (*M* = 12.616) compared to living in both rural and urban environments (moving between) were significant (*M* = 17.572; *M diff* = -4.95, *p* = .03). Similarly, living in an exclusively rural region (*M* = 12.44) compared to living in both rural and urban (moving between) were significant (*M* = 17.572; *M diff* = -5.13, *p* = .03). No differences were found in CD4 means for individuals who did not move in between rural and urban (*M diff* = -.18, *p* = .99). No differences were found for variation in CD4 for moving between urban (*M* = 15.209, *p* = .26) or rural (*M* = 15.295, *p* = .32), nor was it significant for individuals who did not move between urban and rural (*M* = 18.642, *p* = .99).

Hypothesis 5. Hypothesis 5 proposed that over a 2-year period, African American individuals would experience higher incidents of medication non-compliance,

reflected in greater means and variability in viral loads and CD4 counts compared to their counterparts. Results indicate that hypothesis 5 was not supported. Comparisons of viral load means between individuals who identified as African American (M = 8,014) and other identified races (White, non-Latino M = 13,372; Latino M = 4,217; Native American M = < 19; Other M = < 19) showed no differences ($F_{(4,128)} = 0.95$, $p = 0.43$), nor were there differences in variability ($F_{(4,128)} = 1.07$, $p = 0.38$). Similar results occurred for CD4 counts for means ($F_{(4,128)} = 0.77$, $p = 0.55$) and variability ($F_{(4,115)} = 0.32$, $p = 0.86$).

Hypothesis 6. Hypothesis 6 proposed to explore the extent to which each factor (listed below) uniquely predicted medication adherence over two years when controlling for all other factors. To explore a wide-variety of mental health diagnoses, physical health diagnoses, demographic data, and history of substance abuse, we performed multi-model inference analysis to determine the best predictors for mean viral load, variance in viral load, mean CD4 counts, and variance in CD4 counts. To conduct the multiple regression analysis, full multiple regression models were constructed which, included 13 different mental health diagnoses, 15 different physical health diagnoses, 12 aspects of demographic information, and 5 facets of substance abuse history (Table 3), and multi-model inference and model averaging were used to determine the best predictors of mean and variance of viral loads and CD4 counts. The multiple regression models allowed for simultaneous understanding of how different components of mental health, physical health, and lifestyle choices combined to shape treatment adherence.

Overall, results showed that treatment adherence assessed as mean and variance in viral load and CD4 counts was significantly predicted by a combination of mental health,

physical health, and demographic information. For instance, mean viral load was higher in individuals with: a history of alcohol abuse ($F_{(1,123)} = 9.902$, $p = <0.01$), history of memory issues ($F_{(1,123)} = 4.024$, $p = 0.05$), and individuals that moved between Knoxville and rural areas ($F_{(1,123)} = 8.735$, $p = <0.01$). Similarly, individuals with a history of alcohol abuse ($F_{(1,126)} = 6.109$, $p = 0.02$) and individuals that moved between Knoxville and rural areas ($F_{(1,126)} = 3.826$, $p = 0.02$), experienced higher variation in viral loads compared to those who lived exclusively in rural or urban regions, and did not report alcohol abuse. Overall, the best fit model for mean viral load ($F_{(8,123)} = 5.804$, $p < 0.01$) and variation in viral load ($F_{(5, 126)} = 3.914$, $p = <0.01$) explained 23% and 10%, respectively, of the total variation within the viral load dataset, indicating the importance of addressing substance abuse, memory loss and housing stability within this population.

In relation to mean and variation in CD4 counts, individuals with chronic health issues of lung ($F_{(1, 124)} = 6.942$, $p = 0.01$) and eye diseases ($F_{(1, 124)} = 5.451$, $p = 0.02$), and those moving between Knoxville and rural areas ($F_{(2, 124)} = 6.521$, $p = <0.01$) had higher mean CD4 levels and higher variation in CD4 levels, relative to individuals that did not report these conditions. Additionally, individuals with a history of substance abuse ($F_{(1, 125)} = 9.421$, $p = <0.01$), and those that receive less care in their living situation ($F_{(1, 125)} = 4.381$, $p = 0.04$) also experienced higher variability in their CD4 counts compared to controls. The best fit models predicting mean and variation in CD4 counts explained 17% ($F_{(7, 124)} = 4.816$, $p < 0.01$) and 10% ($F_{(6, 127)} = 6.303$, $p < 0.01$) of the total variation in CD4 data, respectively.

As described in the data analytic method section, the above listed factors influencing viral loads and CD4 counts appear to be correlated, thus, the results of the

multiple regression models parameterized a path model to explore the relationship between physical health, mental health, substance abuse history, and demographic data, viral load, and the effect on CD4 counts. See Tables 4-5 for a full list of model parameters and paths not included in this model.

Hypothesis 7. Hypothesis 7 proposed to explore potential mediating effects of mental illness, substance use, physical health, and region on the relationship between race and medication adherence. No mediating factors were found in relation to race, but numerous other significant pathways were discovered. The final averaged multiple regression models were used to parameterize a multi-level path analysis model to better explore the relationships among physical health, mental health, substance abuse history, and demographic data, viral load, and the effect on CD4 counts. Overall, within the best fit path model (AICc = 91.081; Fisher's C = 25.71, $p = 0.69$), 20% of the variation in mean viral load was explained, 15% of the variation in viral load variance, 21% of the variation in mean CD4 counts, and 17% of the variation in CD4 counts (Table 6). Similar to the multiple regression results, it was found that mental health, history of substance abuse, and living conditions were all significant predictors of mean and variation in viral loads and CD4 counts (Figure 2). Additionally, the path model confirmed univariate and multiple regression results in that race/ethnicity was not a significant predictor of viral load (mean - $p = 0.64$, variance - $p = 0.54$) or CD4 count (mean - $p = 0.74$, variance - $p = 0.87$). Contrary to hypothesis 6, it was found that a history of chronic health issues was not retained as a significant predictor of viral load (mean - $p = 0.66$, variance - $p = 0.84$) or CD4 counts (mean - $p = 0.99$, variance - $p = 0.91$) within the best-fit path model (Figure 2).

Individuals whose living situations change between rural and urban environments (coefficient = 7.050, p = <0.01) and individuals with a history of memory loss (coefficient = 4.885, p = 0.01) had significantly higher viral loads relative to individuals who lived exclusively in Knoxville or rural and individuals without memory loss history. Additionally, the best fit model retained a non-significant but trending positive relationship individuals with a substance abuse history (coefficient = 2.182, p = 0.11) and a positive relationship between individuals reporting as religious, but nondenominational (coefficient = 6.638, p = 0.03; Figure 2) and mean viral load. It was found that individuals with a history of substance abuse (coefficient = 3.983, p = 0.03), individuals whose living situations change between rural and urban environments (coefficient = 7.469, p = <0.01), and individuals reporting as Christian (coefficient = 3.709, p = 0.04) had higher variation in their viral loads. Additionally, the best-fit path model retained a non-significant (coefficient = 6.254, p = 0.21), but trending relationship of individuals with memory loss history having higher variation in viral load (Figure 2).

Mean viral load and a history of substance abuse were the best predictors of mean and variation in CD4 counts. Mean CD4 counts were negatively correlated with mean viral load (coefficient = -0. 368, p < 0.01) while individuals that had a history of substance abuse (coefficient = 2.419, p = 0.04) had higher mean CD4 counts relative to individuals without a history of substance abuse (Figure 2). Variance in CD4 counts was best predicted by the variation in viral load (coefficient = 0.200, p = <0.01, Figure 2) and individuals with a history of substance abuse also had higher variation in CD4 counts (coefficient = 3.955, p = <0.01, Figure 2). Additionally, the best fit model retained non-significant relationships between variation in CD4 counts and individuals whose living

situations change between rural and urban environments (coefficient = 2.164, $p = 0.30$), and individuals with a history of memory loss (coefficient = 3.423, $p = 0.36$). Taken together, this path model suggests that integrated health care to address multiple facets of an individual's mental, physical health, substance abuse, and stability in living situation will be the most effective way to ensure treatment adherence.

Chapter 4

Discussion

Human Immunodeficiency Virus (HIV) is a considerable epidemic in the US, especially in the Southeast. Adhering to a medication regiment is highly effective in suppressing the virus and preventing transmission. However, adherence to HIV medication is often inconsistent in the HIV infected population due to multiple factors. Despite research suggesting that factors such as mental health, substance use, physical health comorbidities, regional issues, and race may impact one's medication adherence individually, few studies have assessed multiple factors over time and how they may predict one's likelihood to adhere to medication. The current study aimed to assess how individual factors and the intersection of such factors predict medication adherence, expressed in mean and variability of viral load and CD4 levels.

Hypothesis 1 assessed mental health issues with mean and variation in viral load and CD4 counts over time. When examining mental health factors alone, no significant differences were found between groups. While an effect was expected, this finding presents some interesting considerations. Previous research shows that around half of individuals with HIV were diagnosed with mental illness in certain urban regions (Yehia, 2015). Urban regions are often more resourceful, and may approach treatment for disease in a multidisciplinary manner. This could provide access to thorough mental health screenings, and therefore, accurate diagnoses of mental health issues and co-treatment. Prior clinical trials found improvement of medication adherence when anxiety and depressive symptoms were also treated (Safren et al., 2009), and conversely, that mental health medication with sedating effects took priority over HIV medication

because of obvious side effects (Kalichman et. al., 2015). Though these findings do not reflect previous research, they highlight the effect of HIV medication adherence in those with mental health issues, and presents the possibility that this study's population could be underreporting mental health issues, or that these issues are not thoroughly assessed. This could also relate to gender norms, and the male stigma surrounding mental health. Furthermore, it is possible that the clients in this study underreported mental health, as it is not a requirement to receive continued treatment and services. Interestingly, an effect was found with substance abuse histories (described below), which may be related to mental health issues.

Hypothesis 2 examined whether individuals with substance abuse issues would experience higher incidents of medication non-compliance compared to those not reporting such issues. Results demonstrated that individuals reporting alcohol or drug abuse issues evidenced significantly higher viral variation compared to those not reporting these issues. This finding is incredibly important, as previous research has shown that substance abuse is consistently one of the greatest barriers to HIV medication adherence (Jaquet et al., 2010). Additionally, this population experiences high incidence of substance abuse, with estimates around half of HIV+ individuals and higher rates among aging patients. Though it was hypothesized that substance abuse would cause poor medication adherence, it is also possible that other factors such as undiagnosed mental illness and thus, self-medication with substances, is plausible. Given the insignificant findings about the impact of mental illness on medication adherence in this study, it is difficult to know whether these two factors intersect. In all likelihood, with better mental health screenings and proper diagnoses, an intersecting relationship would

exist with mental illness and substance abuse adversely affecting an individual's ability to follow any medication regimen. Relating back to the mental health findings, this may explain possible underreporting of mental health conditions. Being a primarily male sample, this could suggest that coping with mental health struggles through the use of substances may be possible. Research shows that men often utilize substances for coping instead of seeking professional help (Foster, 2014). The findings from this study underscore the importance of integrating substance use screenings in HIV treatment, and the necessity of using interventions such as medication assisted treatment (MAT) for addiction and therapeutic strategies to address negative coping. Future research could examine the intersection between these substance abuse interventions and HIV medication adherence utilizing this data. A follow-up analysis might provide further insight into the necessity and efficacy of co-treating substance abuse and HIV.

Results from hypothesis 3 found that individuals with chronic physical health issues had greater CD4 variability. This is not a surprising result, as approximately 90% of individuals with HIV have at least one comorbid health condition (Duchane et al., 2013), with aging populations having around four comorbidities on average (Monroe et al., 2013). Though no differences were found for viral variability, suggesting this population was more regimented in their medication, it is logical that other health comorbidities would affect immune response. This was reflected in the variability in CD4 counts, which draws attention to the importance of considering other chronic health conditions in HIV treatment and their impact on overall immune response. The question also arises whether CD4 levels are an accurate representation of HIV+ individuals' immune system or whether other diseases are negatively impactful. Still, CD4 counts, or

immune response, is important to consider in how one's overall health may impact their HIV treatment. This could mean that an individual's baseline immune response may not be functioning at a normal level, and their HIV treatment to become virally suppressed could take longer than those who do not have compromised immune systems. As reported previously, certain health conditions such as eye or lung issues, in conjunction with moving between rural and urban regions, showed greater variability in CD4 counts. Perhaps additional stressors such as housing insecurity, along with a compromised immune system from other chronic health conditions, are predictive of changes in immune response and reflective in CD4 counts.

Hypothesis 4 presented noteworthy findings, where individuals who moved in between rural and urban regions had significant differences from their urban and rural counterparts. These results were different from previous research on urban and rural HIV populations, and may indicate some uniqueness to this study's population. Where previous research suggests that individuals in rural regions do not receive medication treatment nor do they adhere to medications as regularly due to limited care providers, transportation issues, and stigma, this study's population only showed differences when individuals changed regions (HIV surveillance report, 2016). As previously described, HIV+ individuals in Tennessee have unique demographics compared to their fellow Southern equivalents, where the primary group receiving treatment are white MSM (CDC, 2016). This was true within this study's participants. Additionally, there are higher rates of black females who are infected with HIV for reasons that are still unclear, and these demographics trended toward that as well.

The reasons for the urban/rural relocation are unknown, and would be important to investigate further. It is possible that factors related to housing insecurity may influence the change, in combination with changes in access to resources for their care. The directionality of the change was not assessed, which would be equally important to understand. Knowing the impact of urban/rural or rural/urban relocation could help in overall treatment planning.

There were no significant findings for hypothesis 5, which stated that African American/Black individuals would experience higher incidents of medication non-compliance. This does not reflect the national data on HIV medication adherence, and there are several possible reasons for this. As described above, the HIV population in Tennessee is much different than the rest of the Southeast. It is comprised of primarily white MSM, which was reflected in this study. Though there was enough power to assess race as a factor that impacts medication adherence, it is possible that there was not a large enough pool to thoroughly assess for this. As Positively Living has grown over the years and reached individuals who were not engaged in care, it would be important to track demographic factors such as race to assess whether specific minority groups could benefit from additional interventions to adhere to medication. It would be especially important to gain further information on this group, as there are greater cultural influences on behavior in African American/Black men.

Hypotheses 6 and 7 yielded similar results as the primary hypotheses, suggesting that change in location and substance abuse were intersecting factors that were predictive in medication nonadherence. Within the best-fit path model, chronic health issues were not retained as a significant predictor. A unique factor emerged showing that

having a history of memory loss and moving between urban and rural regions was a predictor of medication nonadherence. Memory loss, or neurocognitive decline in HIV+ individuals, is an emerging area of research that is gaining enormous attention. The mechanism behind HIV-related neurocognitive disorder is uncertain, but new research is showing that during early stages of infection, the virus enters the central nervous system, and the longer an individual goes without early medication intervention, the higher risk they have of developing neurocognitive dysfunction or dementia as the disease progresses (Zegarac, 2017). This factor of the study would be incredibly important to assess, as understandably one with memory issues is not likely to remember to adhere to their medication regimen. Understanding the trajectory, in which an individual was infected with HIV to when they obtained treatment and whether they adhered to treatment, could be predictive of medication adherence issues as the disease progresses.

Limitations

The current study had several strengths, including a longitudinal dataset, comparative biological data, and a wealth of demographic information. However, there were also noteworthy limitations to this study. Though the information provided for this study was vast, the majority of the information was self-reported during check-up appointments, and the validity of the data obtained may be skewed. Over-reporting and under-reporting of personal information may have occurred, which could have impacted the results of this study. Additionally, data points were not consistent across clients, as some maintained their 3-month check-ups and others engaged less frequently. Because of this, the data had to be log transformed for homogeneity, and viral load and suppression could not be accurately measured using a longitudinal approach. Since mean and

variability of viral and CD4 variability were assessed instead, some of the results may have been impacted by this methodological issue. The lack of findings with factors such as mental health issues or race and their impact on medication adherence may not necessarily mean there was no effect. This could be due to the analytic approach to the data, which is why further research is necessary.

A further limitation to this study is the assessment of viral load as a measure of medication adherence, which cannot be reported as causality. Though viral loads may be indicators of medication adherence, there are factors that may influence one's viral loads, regardless of how consistently they take their medication. A new area of research surrounding HIV treatment is in genomics, where it is suggestive that an individual's genetic makeup may impact the efficacy of medications. Studies show that the possession or combination of specific genes or lack of certain phenotypes can impact how the body utilizes HIV medication (Obrien & Hendrickson, 2013). Additionally, mutations in the HIV virus can impact both medication response and immune response, which would affect viral loads (Aquaro et al., 2012). Since this level of HIV care is not able to assess genetics or viral mutations and they have enormous impacts on disease progression, we could not conclusively say whether an individual is adhering to their medication or not.

Unfortunately, a significant limitation of this study was the absence of any systematic assessment and collection of this data. As noted before, most items gathered were self-report. Additionally, there were several social workers that were collecting the information from clients, and the consistency and methodology across workers is unknown. Another consideration of these data and overall study is the development and progression of the institute in which it was collected. Positively Living began advertising

their services openly in 2012 due to issues with stigma surrounding HIV treatment and its impact on client engagement. It is likely there were growing pains throughout their evolution, and it should be noted that this data began collection in 2012. Future research could consider controlling for confounding factors such as these.

Future Directions

Research should continue to examine predictive factors for medication nonadherence in HIV populations. Understanding how these factors interconnect could inform interventions treating mental health, substance abuse, chronic health comorbidities, and housing insecurity. For example, if we know an individual seeking treatment for HIV also has a co-occurring substance use or mental health disorder, the individual could be linked to services such as therapy, psychotropic medication, and MAT while simultaneously receiving their HIV treatment. Screening measures for existing and new clients could assess substance abuse problems and/or mental health issues, and a primary care provider or mental health professional could provide treatment for these disorders concurrently with the client's HIV care. Depending on the severity, clients could require inpatient treatment, and the provider could refer the individual directly. Additionally, clients could be prescribed psychotropic medication and MAT alongside their HIV medication. Providers could ensure clients are resourced with outpatient therapy, either in an individual or group setting. This multifaceted approach may help with medication adherence overall, as clients would be receiving numerous avenues of support. Since the conclusion of this study, Positively Living has opened a primary care facility, which offers medical care for infectious disease and preventative

services. Additionally, they have implemented electronic health records (EHR), which would make the continuation of this study feasible.

Thorough assessments of all factors that could impact health should be done using qualified professionals using clinically supported assessment measures. Having this data could drive treatment of comorbidities, and disentangle any possible co-occurring disorders that require treatment. Moreover, in long-term treatment planning, it would be beneficial to utilize neuropsychological testing by a qualified psychologist to gather baseline data on individuals who did not seek HIV treatment after being infected. Obtaining this baseline information upon engagement in treatment would be highly beneficial to have should the individual experience any neurocognitive decline later in life and treatment planning required adjustment. Intervention devices such as medication reminder apps could be used for cases such as these. It would be beneficial to replicate this study or continue with this same population over time.

Furthermore, factors related to gender could be assessed in the future, since this population is primarily male. Utilizing perceptual measures, along with further assessment of issues related to stigma and gender norms may provide insight into medication adherence behaviors. Assessing for internalized homophobia could help explain some of the gender behaviors as well. This information could contribute to research in this area, and drive interventions in the future.

Conclusions

The current study intended to assess multiple factors that could be predictive of medication nonadherence in HIV treatment. Results indicated that individuals with substance abuse issues, changes in residence between urban and rural regions, chronic

health comorbidities, and memory issues have greater variation in viral loads or CD4 counts. Though other hypotheses were not supported, it would be important to continue this research to thoroughly understand the predictive factors that negatively impact HIV medication adherence. Understanding these predictive factors could inform treatment approaches to HIV care, allowing the utilization of a multidisciplinary method. This study may add to the limited research about this specific region and the unique barriers that could impact HIV care. Future research should utilize thorough and clinically supported assessment measures, along with following client care over time.

References

Abbott, L. S., Williams, C. L. (2015). Influences of social determinants of health on African Americans living with HIV in the rural southeast. *Journal of the Association of Nurses in AIDS Care*, 26, 340-356.

Addis, M. E., Mahalik, J. R. (2003). Men, masculinity, and the contexts of help seeking. *American Psychologist*, 58, 5–14.

Anand, P., Springer, S., Copenhaver, M., Altime, F. (2010). Neurocognitive impairment and HIV risk factors: A reciprocal relationship. *AIDS and Behavior*, 14, 1213-26.

Anastos, K., Schneider, M., Gange, S. (2005). The association of race, sociodemographic, and behavioral characteristics with response to highly active antiretroviral therapy in women, *JAIDS*, 39(5), 537–544.

Anonymous. (2015). The HIV epidemic can be stopped. *Nature, 523*(7559), 127.

Auqaro, S., D'Arrigo, R., Svicher, V., Perri, G.D., Caputo, S., Visco-Commandini, U., Santoro, M., Bertoli, A., Mazzotta, F. Bonora, S., Tozzi, V., Bellagamba, R., Zaccarelli, M., Narcisco, P., Perno, C. (2012). Specific mutations in HIV-1 gp41 are associated with immunological success in HIV-1-infected patients receiving enfuvirtide treatment. *Journal of Antimicrobial Chemotherapy,* 58(4), 714-722.

Arnsten, J., Demas, P., Grant, R. (2002). Impact of active drug use on antiretroviral therapy adherence and viral suppression in HIV infected drug users. *Journal of General Internal Medicine*, 17(5), 377–381.

Ajzen, I. (1985). From intentions to actions: A theory of planned behavior. *In J. Kuhl & J. Beckmann (Eds.), Action-control: From cognition to behavior.* 11-39.

Badiee, J., Riggs, P. K., Rooney, A. S., Vaida, F., Grant, I., Atkinson, J. H., Moore, D. J. (2012). Approaches to identifying appropriate medication adherence assessments for HIV infected individuals with comorbid bipolar disorder. *AIDS patient care and STDs, 26*(7), 388. doi:10.1089/apc.2011.0447

Baligh, Y., Stevens-Shield, A., Momplaiser, F., Taylor, L., Gross, R., Brady, K. (2015). Health outcomes of HIV-infected people with mental illness. *AIDS and Behavior,* 19(8), 1491-1500.

Barasa, S. S. (2011). True story about HIV: Theory of viral sequestration and reserve infection. *HIV/AIDS - Research and Palliative Care, 3*, 125-133. doi:10.2147/HIV.S26578

Belenky, N., Cole, S., Pence, B., Itemba, D., Maro, V., Whetten, K. (2014). Depressive Symptoms, HIV Medication Adherence, and HIV Clinical Outcomes in Tanzania: A Prospective, Observational Study. *PLoS ONE, 9*(5), E95469.

Berger, M., Sullivan, K., Parnell, H., Keller, J., Pollard, A., Cox, M., Quinlivan, E. (2016). Barriers and Facilitators to Retaining and Reengaging HIV Clients in Care. *Journal of the International Association of Providers of AIDS Care (JIAPAC), 15*(6), 486-493.

Blake, B. J., Taylor, G. A. J., & Sowell, R. L. (2017). Exploring Experiences and Perceptions of Older African American Males Aging With HIV in the Rural Southern United States. *American Journal of Mens Health, 11*(2), 221-232. doi:10.1177/1557988316662875

Blank, M., Mandell, D., Aiken, L., Hadley, T. (2002). Co-occurrence of HIV and serious mental illness among Medicaid recipients. *Psychiatric Services*, 53(7), 868-873.

Buchanan, A. L., Montepiedra, G., Sirois, P. A., Kammerer, B., Garvie, P. A., Storm, D. S., Nichols, S. L. (2012). Barriers to medication adherence in HIV-infected children and youth based on self- and caregiver report. *Pediatrics, 129*(5), e1244. doi:10.1542/peds.2011-1740

By, M., Michael, H. (2012). ADVANCING REASONED ACTION THEORY: A Reasoned Action Approach to HIV Prevention for Persons with Serious Mental Illness. *Annals of the American Academy of Political and Social Science, 640*, 173-173.

Carey, M., Carey, K., Maisto, S., Schroder, K., Vanable, P., Gordon. C. (2004). HIV risk behavior among psychiatric outpatients. *Journal of Nervous & Mental Disease,* 192(4), 289-96.

Carolyn, M. A., Catherine, C. M., Kenneth, A. W., & Aaron, M. K. Relationship between HIV stigma and self-isolation among people living with HIV in Tennessee. *PLoS ONE, 8*(8), e69564. doi:10.1371/journal.pone.0069564

Chama, S., & Ramirez, O. (2014). Psychosocial challenges of young people affected by HIV: experiences from Hamilton County, Chattanooga, Tennessee. *AIDS Care*, 1-7. doi:10.1080/09540121.2014.989807

Chandra, A., Scott, M. M., Jaycox, L. H., Meredith, L. S., Tanielian, T., Burnam, A. (2009). Racial/ethnic differences in teen and parent perspectives toward depression treatment. *Journal of Adolescent Health*, 44, 546–553.

Cochran, S. D., Sullivan, J. G., & Mays, V. M. (2003). Prevalence of mental disorders, psychological distress, and mental services use among lesbian, gay, and

bisexual adults in the United States. *Journal of Consulting and Clinical Psychology*, 71, 53–61.

Cohen J. (1988). Statistical Power Analysis for the Behavioral Sciences. New York, NY: Routledge Academic

Cohn, S., Jiang, H., McCutchan, J. (2011). Association of ongoing drug and alcohol use with non-adherence to antiretroviral therapy and higher risk of AIDS and death: results from ACTG 362. *AIDS Care*, 23, 775–85.

Collins, P., Holman, A., Freeman M., Patel, V. (2006). What is the relevance of mental health to HIV/AIDS care and treatment programs in developing countries? A systematic review, *AIDS*, 1571–1582.

Collins, P., Patel, V., Joestl, S., March, D., Insel, T. (2011) Grand challenges in global mental health, *Nature*, 475(7354), 27–30.

Cook, J., Grey, D., Burke-Miller, J. (2006). Effects of treated and untreated depressive symptoms on highly active antiretroviral therapy use in a US multi-site cohort of HIV-positive women. *AIDS Care*, 18(2), 93–100.

Costelloe, S., Kemppainen, J., Brion, J., Mackain, S., Reid, P., Frampton, A., Rigsbee, E. (2015). Impact of anxiety and depressive symptoms on perceptions of stigma in persons living with HIV disease in rural versus urban North Carolina. *AIDS Care*, 1-4. doi:10.1080/09540121.2015.1114993

Crepaz, N., Marks, G. (2002). Towards an understanding of sexual risk behavior in people living with HIV: a review of social, psychological, and medical findings. *AIDS*, 16(2), 135–149.

Dale, S. K., Bogart, L. M., Wagner, G. J., Galvan, F. H., & Klein, D. J. (2016). Medical mistrust is related to lower longitudinal medication adherence among African-American males with HIV. *Journal of Health Psychology, 21*(7), 1311-1321. doi:10.1177/1359105314551950

Davis J., Bynum, S., Katz, RV. (2012) Sociodemographic differences in fears and mistrust contributing to unwillingness to participate in cancer screenings. *Journal of Health Care for the Poor and Underserved*, 23, 67–76.

Dickerson, F., Brown, C., Kreyenbuhl. J., Goldberg, R., Juan Fang, L., Dixon, L. (2004). Sexual and reproductive behaviors among persons with mental illness. *Psychiatric Services*, 55(11), 1299-1301.

Domanico, R., & Crawford, I. (2000). Psychological Distress Among HIV-Impacted African-American and Latino Males. *Journal of Prevention & Intervention in the Community, 19*(1), 55-78. doi:10.1300/J005v19n01_04

Doshi, R., Milberg, J., Isenberg, D., Matthews, T., Malitz, F., Matosky, M. Cheever, L. (2015). High Rates of Retention and Viral Suppression in the US HIV Safety Net System: HIV Care Continuum in the Ryan White HIV/AIDS Program, 2011. *Clinical Infectious Diseases, 60*(1), 117-125.

Duncan, A., Vandevanter, N., Ahmed, R., Burrell-Piggott, T., & Furr-Holden, C. D. (2014). The role of substance use in adherence to HIV medication and medical appointments. *The Journal of the Association of Nurses in AIDS Care : JANAC, 25*(3), 262. doi:10.1016/j.jana.2013.11.001

Edun, B., Iyer, M., Albrecht, H., & Weissman, S. (2017). The South Carolina rural–urban HIV continuum of care. *AIDS Care, 29*(7), 817-822. doi:10.1080/09540121.2016.1270397

Feller, D., Agins, B. (2017). Understanding Determinants of Racial and Ethnic Disparities in Viral Load Suppression. *Journal of the International Association of Providers of AIDS Care (JIAPAC), 16*(1), 23-29.

Gao, X., Nau, D., Rosenbluth, S., Scott, V., Woodward, C. (2000). The relationship of disease severity, health beliefs and medication adherence among HIV patients. *AIDS Care*, 13, 387–398.

Gardner, E., Sharma, S., Peng, G. (2008). Differential adherence to combination antiretroviral therapy is associated with virological failure with resistance, *AIDS*, 22(1), 75–82.

Gaston, G. B. (2013). African-Americans perceptions of health care provider cultural competence that promote HIV medical self-care and antiretroviral medication adherence. *AIDS Care, 25*(9), 1159-1165. doi:10.1080/09540121.2012.752783

Goldberg, R. W. (2004). Hepatitis and HIV screening, education, and treatment for adults with serious mental illness. In (Vol. 26, pp. 167-168).

Gonzalez, A., Barinas, J., O'Cleirigh, C. (2011). Substance use: impact on adherence and HIV medication treatment. *Current HIV/AIDS Report*, 8, 223–34.

Gonzalez, J., Batchelder, A., Psaros, C., Safren, S. (2011). Depression and HIV/AIDS treatment nonadherence: a review and meta-analysis. *Journal of Acquired Immune Deficiency Syndrome*, 58, 181–7.

Gonzalez, A., Mimiaga, M., Israel, J., Andres Bedoya, C., & Safren, S. (2013). Substance Use Predictors of Poor Medication Adherence: The Role of Substance Use Coping Among HIV-Infected Patients in Opioid Dependence Treatment. *AIDS and Behavior, 17*(1), 168-173. doi:10.1007/s10461-012-0319-6

Good, G. (1989). Male Role and Gender Role Conflict: Relations to Help Seeking in Men. *Journal of Counseling Psychology, 36*(3), 295-300.

Goulet, J., Fultz, S., Rimland , D., Butt, A, Gibert, C. (2007). Aging and infectious diseases: do patterns of comorbidity vary by HIV status, age, and HIV severity? *Clinical Infectious Disease*, 45(12), 1593–1601.

Gray, S. C., Massaro, T., Chen, I., Edholm, S. J., Grotheer, R., Zheng, Y., Chang, H. H. (2016). A county-level analysis of persons living with HIV in the southern United States. *AIDS Care*, 28, 266-272.

Griffith, D. M., Allen, J. O., & Gunter, K. (2011). Social and Cultural Factors Influence African American Mens Medical Help Seeking. *Research on Social Work Practice, 21*(3), 337-347. doi:10.1177/1049731510388669

Grueber, C. E., Nakagawa, S., Laws, R. J., & Jamieson, I. G. (2011). Multimodel inference in ecology and evolution: challenges and solutions. *Journal of Evolutionary Biology*, *24*(4), 699–711.

Hammer, J. H., Vogel, D. L., & Heimerdinger-Edwards, S. R. (2013). Mens Help Seeking: Examination of Differences Across Community Size, Education, and Income. *Psychology of Men & Masculinity, 14*(1), 65-75. doi:10.1037/a0026813

Hausmann, L., Kwoh, C., Hannon, M. (2013) Perceived racial discrimination in health care and race differences in physician trust. *Race and Social Problems*, 5, 113–120.

Heaton, R., Franklin, D., Ellis, R., McCutchan, J., Letendre, S. (2011). HIV-associated neurocognitive disorders before and during the era of combination antiretroviral therapy: differences in rates, nature, and predictors. *Journal of Neurovirology*, 17(1), 141-150.

Hinkin, C., Castellon, S., Atkinson, J., Goodkin, K. (2001). Neuropsychiatric aspects of HIV infection among older adults, *Journal of Clinical Epidemiology*, 54(1), 44–52.

HIV Surveillance Report, 2011-2018, Washington, DC: Centers for Disease Control and Prevention (CDC).

Hogg, R., Heath, K., Yip, K. (1998). Improved survival among HIV-infected individuals following initiation of antiretroviral therapy. *Journal of American Medical Association*, 279(6), 450-454.

Huang, Y. (2013). Segmental modeling of viral load changes for HIV longitudinal data with skewness and detection limits. *Statistics in Medicine, 32*(2), 319-334. doi:10.1002/sim.5527

Jaquet, A,. Ekouevi, D., Bashi, J., Aboubakrine, M., Messou E. (2010). Alcohol use and non-adherence to antiretroviral therapy in HIV-infected patients in West Africa. *Addiction*, 105(8), 1416–1421.

Justman, J., & El-Sadr, W. M. (2012). Stemming the U.S. HIV epidemic: act local. *Science (New York, N.Y.), 337*(6093), 411. doi:10.1126/science.337.6093.411

Kaaya, S., Eustache, E., Lapidos-Salaiz, I., Musisi, S., Psaros, C., & Wissow, L. (2013). Grand Challenges: Improving HIV Treatment Outcomes by Integrating Interventions for Co-Morbid Mental Illness. *10*(5), e1001447. doi:10.1371/journal.pmed.1001447

Kalichman, S., Pellowski, J., Kegler, C., Cherry, C., & Kalichman, M. (2015b). Medication adherence in people dually treated for HIV infection and mental health conditions: test of the medications beliefs framework. *Journal of Behavioral Medicine, 38*(4), 632-641. doi:10.1007/s10865-015-9633-6

Kolmodin MacDonell, K., J. Jacques-Tiura, A., Naar, S., & Isabella Fernandez, M. (2016). Predictors of Self-Reported Adherence to Antiretroviral Medication in a Multisite Study of Ethnic and Racial Minority HIV-Positive Youth. *Journal of Pediatric Psychology, 41*(4), 419-428. doi:10.1093/jpepsy/jsv097

Konkle‐Parker, D. J., Erlen, J. A., Dubbert, P. M., & May, W. (2012). Pilot testing of an HIV medication adherence intervention in a public clinic in the Deep South. *Journal of the American Academy of Nurse Practitioners, 24*(8), 488-498. doi:10.1111/j.1745-7599.2012.00712

Kosiba, J., Gonzalez, A., O'Cleirigh, C., & Safren, S. (2014). Medication Adherence and HIV Symptom Distress in Relation to Panic Disorder Among HIV-Positive Adults Managing Opioid Dependence. *Cognitive Therapy and Research, 38*(4), 458-464. doi:10.1007/s10608-014-9608-x

Krentz, H., Cosman, I., Lee, K., Ming, J., Gill, M. (2012). Pill burden in HIV infection: 20 years of experience. *Antiviral Therapy*. 13, 833–840.

Lefcheck, J. S. (2016). piecewiseSEM: Piecewise structural equation modelling in r for ecology, evolution, and systematics. *Methods in Ecology and Evolution*, *7*(5), 573–579.

Liu, H., Longshore, D., Williams, J. (2006). Substance abuse and medication adherence among HIV-positive women with histories of child sexual abuse, *AIDS Behavior*, 10(3), 279–286.

Lucey, B., Clifford, D., Creighton, J., Edwards, R., McArthur, J., & Haythornthwaite, J. (2011). Relationship of depression and catastrophizing to pain, disability, and medication adherence in patients with HIV-associated sensory neuropathy. *AIDS Care, 23*(8), 921-928. doi:10.1080/09540121.2010.543883

Machtinger, E., Wilson, T., Haberer, J., Weiss, D. (2012). Psychological trauma and PTSD in HIV-positive women: a meta-analysis, *AIDS Behavior*, 16(8), 2091–2100.

Magovcevic, M., Addis, M. E. (2005). Linking gender-role conflict to nonnormative and self-stigmatizing perceptions of alcohol abuse and depression. *Psychology of Men & Masculinity*, 6, 127–136.

Mahalik, J. R., Lagan, H. D., Morrison, J. A. (2006). Health behaviors and masculinity in Kenyan and U.S. male college students. *Psychology of Men and Masculinity*, 7, 191–202.

Mahalik, J. R., Locke, B. D., Ludlow, L. H., Deimer, M. A., Scott, R. P. J., Gottfried, M., Freitas, G. (2003). Development of the Conformity to Masculine Norms Inventory. *Psychology of Men and Masculinity*, 4, 3–25.

Mahalik, J. R., Pierre, M. R., Wan, S. S. C. (2006). Examining racial identity and masculinity as correlates of self-esteem and psychological distress in Black men. *Journal of Multicultural Counseling and Development*, 34, 94–104.

Maj, M., Janssen, R., Starace, F., Zaudig, M., Satz, P. (1994). WHO neuropsychiatric AIDS study, cross-sectional Phase-I - Study design and psychiatric findings. *Archives of General Psychiatry*, 51(1), 39–49.

Marx, P. A., Drucker, E. M., & Schneider, W. H. (2011). The serial passage theory of HIV emergence. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, 52*(3), 421. doi:10.1093/cid/ciq166

Malow, R., Devieux, J., Stein, J. (2013). Depression, substance abuse and other contextual predictors of adherence to antiretroviral therapy(ART) among Haitians. *AIDS Behavior*, 17(4), 1221–1230.

Mayston, R., Kinyanda, E., Chishinga, N., Prince, M., Patel, V. (2012). Mental disorder and the outcome of HIV/AIDS in low-income and middle-income countries: a systematic review. *AIDS* 26(Suppl 2), 117–135.

McGregor, S., Henderson, K. J., & Kaldor, J. M. (2015). Capacity building in longitudinal HIV research. In (Vol. 3, pp. e18-e19).

Monroe, A. K., Pena, J. S., Moore, R. D., Riekert, K. A., Eakin, M. N., Kripalani, S., & Chander, G. (2017). Randomized controlled trial of a pictorial aid intervention for medication adherence among HIV-positive patients with comorbid diabetes or hypertension. *AIDS Care*, 1-8. doi:10.1080/09540121.2017.1360993

Monroe, A. K., Rowe, T. L., Moore, R. D., & Chander, G. (2013). Medication adherence in HIV-positive patients with diabetes or hypertension: a focus group study. *BMC health services research, 13*, 488. doi:10.1186/1472-6963-13-488

Moore, D., Blackstone, K., Woods, S. P., Ellis, R., Atkinson, J. H., Heaton, R., The Hnrc Group And The Tmarc Group, I. (2012). Methamphetamine use and neuropsychiatric factors are associated with antiretroviral non-adherence. *AIDS Care, 24*(12), 1504-1513. doi:10.1080/09540121.2012.672718

Moore, D., Posada, C., Parikh, M., Arce, M., Vaida, F., Riggs, P., Atkinson, J. (2012). HIV-Infected Individuals with Co-occurring Bipolar Disorder Evidence Poor Antiretroviral and Psychiatric Medication Adherence. *AIDS and Behavior, 16*(8), 2257-2266. doi:10.1007/s10461-011-0072-2

Moore, J. O., Hardy, H., Skolnik, P. R., & Moss, F. H. (2011). A collaborative awareness system for chronic disease medication adherence applied to HIV infection, 1523-1527.

Mugavero, M., Ostermann, J., Whetten, K. (2006). Barriers to antiretroviral adherence: the importance of depression, abuse, and other traumatic events. *AIDS Patient Care STDS*, 20(6), 418–428.

Murphy, E., Collier A., Kalish L. (2001). Highly active antiretroviral therapy decreases mortality and morbidity in patients with advanced HIV disease. *Annals of Internal Medicine*, 135(1),17-26

Nadya, M. B., Stephen, R. C., Brian, W. P., Dafrosa, I., Venance, M., & Kathryn, W. Depressive symptoms, HIV medication adherence, and HIV clinical outcomes in Tanzania: a prospective, observational study. *PLoS ONE, 9*(5), e95469. doi:10.1371/journal.pone.0095469

Nakagawa, S., & Schielzeth, H. (2013). A general and simple method for obtaining R2 from generalized linear mixed-effects models. *Methods in Ecology and Evolution*, *4*(2), 133–142.

O'Brien, S. J., & Hendrickson, S. L. (2013). Host genomic influences on HIV/AIDS. *Genome biology*, *14*(1), 201. doi:10.1186/gb-2013-14-1-201

Ohl, M. E., & Perencevich, E. (2011). Frequency of human immunodeficiency virus (HIV) testing in urban vs. rural areas of the United States: Results from a nationally-representative sample. *BMC Public Health, 11*, 681.

Ojcius, D. (2007). HIV theory challenged. *Nature reviews. Microbiology, 5*(8), 574-575. doi:10.1038/nrmicro1721

Okonsky, J. (2011). Problems taking pills: understanding HIV medication adherence from a new perspective. *AIDS Care, 23*(12), 1652-1659. doi:10.1080/09540121.2011.579944

Oksanen, J., Blanchet, F. G., Kindt, R., Legendre, P., O'hara, R. B., Simpson, G. L., Wagner, H. (2010). Vegan: community ecology package. R package version 1.17-4. *Http://Cran. r-Project. Org>. Acesso Em*, *23*, 2010.

Owe-Larsson, B., Sall, L., Salamon, E., Allgulander, C. (2009). HIV infection and psychiatric illness. *African Journal of Psychiatry*, 12, 115–128.

Panos, S. E., Del Re, A. C., Thames, A. D., Arentsen, T. J., Patel, S. M., Castellon, S. A., Hinkin, C. H. (2014). The impact of neurobehavioral features on medication adherence in HIV: Evidence from longitudinal models. *AIDS Care, 26*(1), 79-86. doi:10.1080/09540121.2013.802275

Parsons, J., Kowalczyk, W., Botsko, M., Tomassilli, J., & Golub, S. (2013). Aggregate Versus Day Level Association Between Methamphetamine Use and HIV Medication Non-adherence Among Gay and Bisexual Men. *AIDS and Behavior, 17*(4), 1478-1487. doi:10.1007/s10461-013-0463-7

Parsons, J. T., Starks, T. J., Millar, B. M., Boonrai, K., & Marcotte, D. (2014). Patterns of substance use among HIV-positive adults over 50: implications for treatment and medication adherence. *Drug and alcohol dependence, 139*, 33. doi:10.1016/j.drugalcdep.2014.02.704

Patel, R., Kassaye, S., Gore-Felton, C., Wyshak, R., Kadzirange, C. (2009). Quality of life, psychosocial health, and antiretroviral therapy among HIV-positive women in Zimbabwe, *AIDS Care* 21(12), 1517–1527.

Pellowski, J. A., Kalichman, S. C., Kalichman, M. O., & Cherry, C. (2016). Alcohol-antiretroviral therapy interactive toxicity beliefs and daily medication adherence and alcohol use among people living with HIV. *AIDS Care, 28*(8), 963-970. doi:10.1080/09540121.2016.1154134

Phillips, K. D. (2007). Social support, coping, and medication adherence among HIV-Positive women with depression living in rural areas of the southeastern United States. In: SelectedWorks.

Pinheiro, J., Bates, D., DebRoy, S., & Sarkar, D. (2017). R Core Team (2014) nlme: linear and nonlinear mixed effects models. R package version 3.1-118. *R Foundation for Statistical Computing, Vienna*.

R Core Development Team. (2008). R: A language and environment for statistical computing. Retrieved from http://www.r-project.org

RStudio Team. 2013. RStudio: integrated development for R. RStudio, Boston, Massachusetts, USA.

Reif, S., Proeschold-Bell, R., Yao, J., Legr, Uehara, A., Asiimwe, E., & Quinlivan, E. (2013). Three types of self-efficacy associated with medication adherence in patients with co-occurring HIV and substance use disorders, but only when mood disorders are present. *Journal of Multidisciplinary Healthcare, 6*, 229-237.

Reif, S., Whetten, K., & Wilson, E. (2011). *HIV/AIDS Epidemic in the south reaches crisis proportions in last decade*. Duke Center for Health Policy and Inequalities Research.

Robertson, K., Liner, J., Heaton, R. (2009). Neuropsychological Assessment of HIV-Infected Populations in International Settings. Netherlands: Springer. *Neuropsychology Review*, 232–248.

Rosenberg, S., Goodman, L., Osher, F., Swartz, M., Essock, S., Butterfield, M., Constantine, N., Wolford, G., Salyers. M. (2001). Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness (SMI). *American Journal of Public Health*, 91(1), 31-37.

Rosenstock, I.M. (1960). What research in motivation suggests for public health. *In American Journal of Public Health.* 50, 295-302.

Rothbard, A., Blank, M., Staab, J., TenHave, T., Young, D., Berry, S., Eachus, S. (2009). Previously undetected metabolic syndromes and infectious diseases among psychiatric inpatients. *Psychiatric Services*, 60(4), 534-37.

Safren, S., O'Cleirigh, C., Tan, J. (2009). A randomized controlled trial of cognitive behavioral therapy for adherence and depression (CBT-AD) in HIV-infected individuals. *Health Psychology*, 28(1), 1–10.

Schonnesson, L., Williams, M., Ross, M., Bratt, G., Keel, B. (2007). Factors associated with suboptimal antiretroviral therapy adherence to dose, schedule, and dietary instructions, *AIDS Behavior*, 11(2), 175–183.

Shavers, V., Lynch, C., Burmeister, L. (2002). Racial differences in factors that influence the willingness to participate in medical research studies. *Annals of Epidemiology*. 12(4), 248–256.

Sherbourne, C., Hays, R., Fleishman, J., Vitiello, B., Magruder, K. (2000). Impact of psychiatric conditions on health-related quality of life in persons with HIV infection. *American Journal of Psychiatry*, 157(2), 248–254.

Shipley, B. (2009). Confirmatory path analysis in a generalized multilevel context. *Ecology*, *90*(2), 363–368.

Shipley, B. (2013). The AIC model selection method applied to path analytic models compared using ad-separation test. *Ecology*, *94*(3), 560–564.

Shuper, P., Neuman, M., Kanteres, F., Baliunas, D., Joharchi, N. (2010). Causal considerations on alcohol and HIV/AIDS–a systematic review, *Alcohol and Alcoholism* 45(2), 159–166.

Sierra Hernandez, C. A., Han, C., Oliffe, J. L., & Ogrodniczuk, J. S. (2014). Understanding Help-Seeking Among Depressed Men. *Psychology of Men; Masculinity, 15*(3), 346-354. doi:10.1037/a0034052

Simoni J., Huh, D., Wilson, I. (2012). Racial/ethnic disparities in ART adherence in the United States: Findings from the MACH14 study. *Journal of Acquired Immune Deficiency Syndromes*, 60, 466–472.

Spire, B., Lucas, G., Carrier, M. (2007). Adherence to HIV treatment among IDUs and the role of opioid substitution treatment (OST). *International Journal on Drug Policy*. 18, 262–70.

Starks, T. (2017) Preintervention Profiles of Information, Motivational, and Behavioral Self-Efficacy for Methamphetamine Use and HIV Medication Adherence Among Gay and Bisexual Men. *AIDS Weekly*, 133.

Stephens, J., Artiga, S., & Paradise, J. (2014). Health coverage and care in the south in 2014 and beyond. Retrieved from http://kff.org/disparities-policy/issue-brief/health-cover-age-and-care-in-the-south-in-2014-and-beyond/.

Stewart, K. E., Diclemente, R. J., & Ross, D. (1999). Adolescents and HIV: theory‐based approaches to education of nurses. *Journal of Advanced Nursing, 30*(3), 687-696. doi:10.1046/j.1365-2648.1999.01118.

Surratt, H. L., Grady, C. L., Levi-Minzi, M. A., & Kurtz, S. P. (2014). Medication adherence challenges among HIV positive substance abusers: the role of food and housing insecurity. *AIDS Care*, 1-8. doi:10.1080/09540121.2014.967656

Sutton, M., Anthony, M. N., Vila, C., McLellan-Lemal, E., Weidle, P. J. (2010). HIV testing and HIV/AIDS treatment services in rural counties in 10 southern states: Service provider perspectives. *Journal of Rural Health*, *26*(3), 240–247.

Sweeney, S. M., & Vanable, P. A. (2014). Impact of HIV-related stigmatization on medication adherence in HIV-positive individuals. *Annals of Behavioral Medicine, 47*, 259.

Thames, A., Moizel, J., Panos, S. (2012). Differential predictors of medication adherence in HIV: findings from a sample of African American and Caucasian HIV-positive drug-using adults. *AIDS Patient Care STDS*, 26(10), 621–630.

Tucker, J., Burnam, M., Sherbourne, C., Kung, F., Gifford, A. (2003). Substance use and mental health correlates of nonadherence to antiretroviral medications in a sample of patients with human immunodeficiency virus infection. *American Journal of Medicine*,114(7), 573–580.

Tucker, J., Orlando, M., Burnam, M., Sherbourne, C., Kung, F., Gifford, A. (2004). Psychosocial mediators of antiretroviral nonadherence in HIV-positive adults with substance use and mental health problems. *Health Psychology*, 23(4), 363–370.

Tyer‐Viola, L., Corless, I., Webel, A., Reid, P., Sullivan, K., & Nichols, P. (2014). Predictors of Medication Adherence Among HIV‐Positive Women in North America. *Journal of Obstetric, Gynecologic, & Neonatal Nursing, 43*(2), 168-178.

Van Sighem, A., Van de Wiel M., Ghani A. (2003). Mortality and progression to AIDS after starting highly active antiretroviral therapy. *AIDS*, 17(15), 2227-2236.

Vogel, D. L., Heimerdinger-Edwards, S., Hammer, J. H., Hubbard, A. (2011). "Boys don't cry": Examination of the links between endorsement of masculine norms, self-stigma and help-seeking attitudes for men from diverse backgrounds. *Journal of Counseling Psychology*, 58, 368-382.

Vogel, D. L., Shechtman, Z., Wade, N. G. (2010). The role of public and self-stigma in predicting attitudes toward group counseling. *The Counseling Psychologist*, 38, 904-922.

Vogel, D. L., Wade, N. G., Ascheman, P. (2009). Measuring perceptions of stigmatization by others for seeking psychological help: Reliability and validity of a new stigma scale with college students. *Journal of Counseling Psychology*, 56, 301–308.

Vogel, D. L., Wade, N., Haake, S. (2006). Measuring the self-stigma associated with seeking psychological help. *Journal of Counseling Psychology*, 53, 325–337.

Vogel, D. L., Wade, N., Hackler, S. (2007). Perceived public stigma and the willingness to seek counseling: The mediating role of self-stigma and attitudes toward counseling. *Journal of Counseling Psychology*, 54, 40 –50.

Wagner, G., Kanouse, D., Koegel, P., Sullivan, G. (2003). Adherence to HIV antiretrovirals among persons with serious mental illness. *AIDS Patient Care STDS*, 17(4), 179–186.

Walensky R., Paltiel A., Losina E. (2006). The survival benefits of AIDS treatment in the United States. *Journal of Infectious Disease*. 194(1), 11-19.

Webel, A. R., Longenecker, C. T., Gripshover, B., Hanson, J. E., Schmotzer, B. J., & Salata, R. A. (2014). Age, stress, and isolation in adults living with HIV. *AIDS Care*, 26, 523-531.

Weissman, S. A., Duffus, W. V., Iyer, M., Chakraborty, H., Samantapudi, A., Albrecht, H. (2015). Rural–Urban Differences in HIV Viral Loads and Progression to AIDS among New HIV Cases. *Southern Medical Journal, 108*(3), 180-188.

Wester, C., Rebeiro, P., Shavor, T., Shepherd, B., McGoy, S., Daley, B., Pettit, A. (2016). The 2013 HIV Continuum of Care in Tennessee. *Public Health Reports, 131*(5), 695-703.

Westergaard, R.P., Beach, M.C., Saha, S. et al., *Journal of Internal Medicine*, (2014) 29: 140.

Whetten, K., Reif, S., Napravnik, S., Swartz, M., Thielman, N., Eron, J., Soto, T. (2005). Substance abuse and symptoms of mental illness among HIV-positive persons in the Southeast. *Southern Medical Journal, 98*(1), 9-14.

Williams, E. A., Kanu, M., Williams, C., Jackman, R. M., Alsup, P., Theriot, R., & Wong, S. P. (2010). Tennessee HIV/AIDS People of Color Project. *Journal of Health Care for the Poor and Underserved, 21*(3), 1046-1059. doi:10.1353/hpu.0.0339

Willie, T. C., Overstreet, N. M., Sullivan, T. P., Sikkema, K. J., & Hansen, N. B. (2015). Barriers to HIV Medication Adherence: Examining Distinct Anxiety and Depression Symptoms among Women Living with HIV Who Experienced Childhood Sexual Abuse. *Behavioral Medicine*. doi:10.1080/08964289.2015.1045823

Wilson, L., Korthuis, T., Fleishman, J., Conviser, R., Lawrence, P., Moore, R., & Gebo, K. (2011). HIV-related medical service use by rural/urban residents: a

multistate perspective. *AIDS Care, 23*(8), 971-979. doi:10.1080/09540121.2010.543878

Yehia, B., Stephens-Shields, A., Fleishman, J., Berry, S., Agwu, A., Metlay, J., Gebo., K. (2015). The HIV Care Continuum: Changes over Time in Retention in Care and Viral Suppression. *PLoS ONE, 10*(6), E0129376

Yun, L., Maravi, M., Kobayashi, J., Barton, P., Davidson, A. (2005). Antidepressant treatment improves adherence to antiretroviral therapy among depressed HIV-infected patients, *JAIDS*, 38(4), 432–438.

Zegarac, J. (2017) Assessing the risk factors of neurocognitive decline in HIV+ individuals. *Infectious Disease National Advisor.*

Appendix

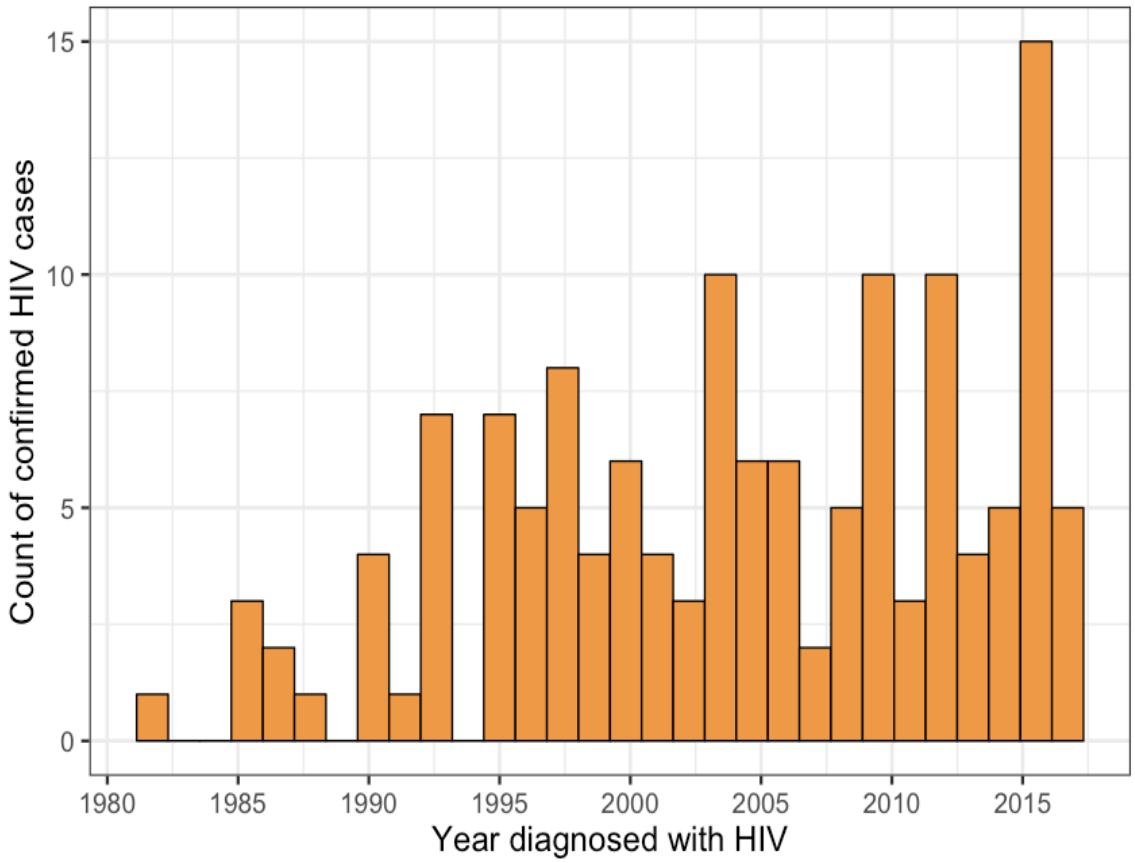


Figure 1. Diagnosis by year

Table 1. Viral load parameters

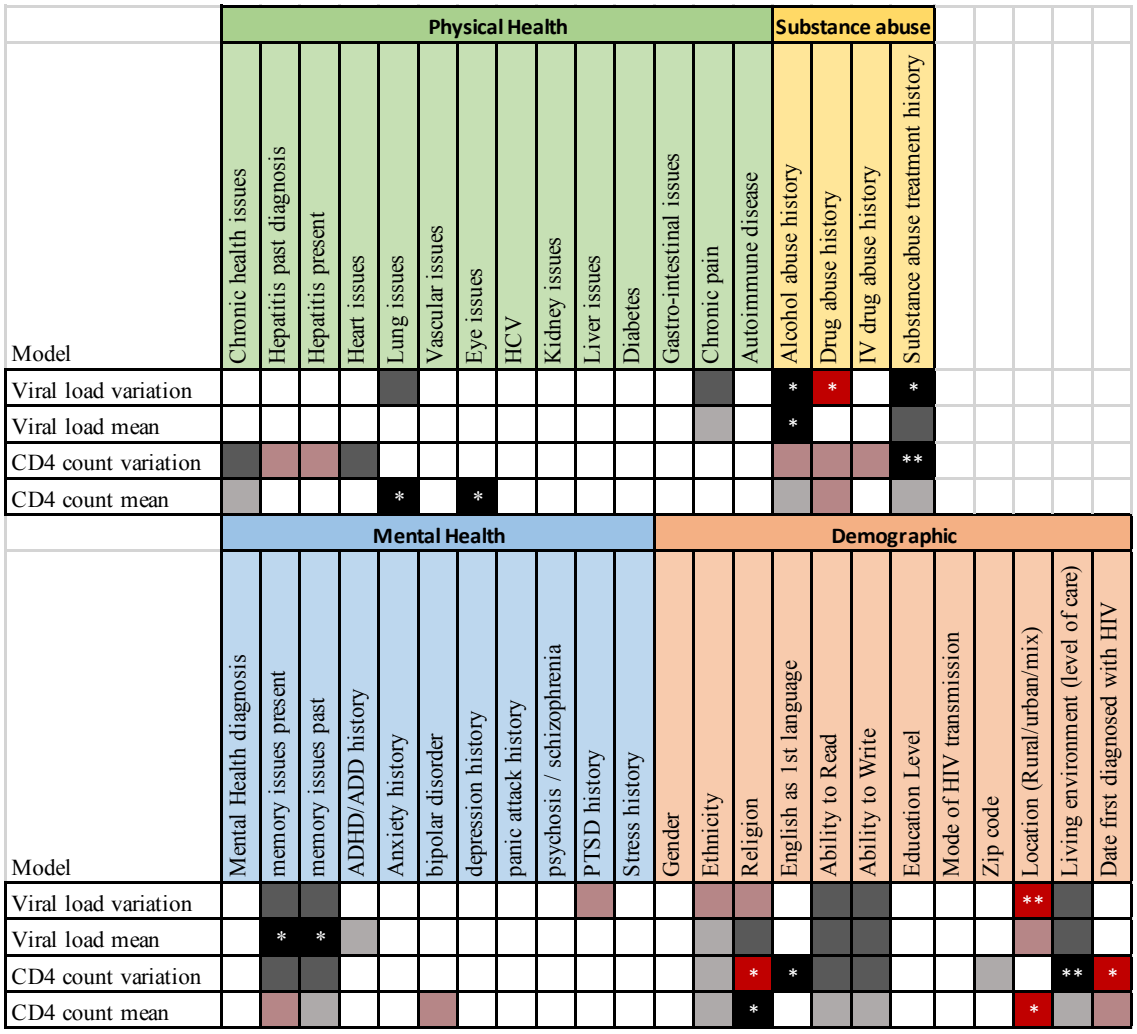
Factor	Response	Mean viral load	Viral load SD	Viral load range	Viral load variation	Viral load variance SD	Viral load variance range
mental health trt.	No	14143.70	45938.2	(18.5, 242520)	2.1E+09	1.2E+10	(0, 8.3E+10)
	Yes	9447.33	27592.3	(14.6, 164500)	1.67E+09	9.1E+10	(0, 8.3E+10)
Alcohol abuse hist.	No	12093.81	39108.1	(14.6, 242520)	2.0E+09	1.2E+10	(0, 8.3E+10)
	Yes	8639.79	22280.2	(16.9, 89906)	1.4E+09	4.0E+09	(0, 1.7E+10)
Drug abuse hist.	No	9637.67	32224.3	(14.6, 242520)	3.7E+08	1.4E+09	(0, 8.5E+10)
	Yes	15065.83	42087.8	(18.5, 185699.7)	5.7E+09	1.9E+10	(0, 8.3E+10)
IV drug abuse hist.	No	12014.79	37073.5	(14.6, 242520)	2.0E+09	1.1E+10	(0, 8.3E+10)
	Yes	4468.32	12169.4	(19, 48809.5)	3.5E+08	1.2E+09	(0, 4.8E+09)
Chronic Health iss.	No	13357.84	43168.3	(18.5, 242520)	1.8E+09	1.2E+10	(0, 8.3E+10)
	Yes	9707	29157.8	(14.6, 164500)	1.8E+09	9.3E+09	(0, 8.1E+10)
Chronic Pain iss.	No	11114.79	36606.8	(16.9, 242520)	1.3E+09	8.7E+09	(0, 8.3E+10)
	Yes	11087.34	31405.5	(14.6, 153180.3)	3.1E+09	1.3E+10	(0, 8.1E+10)
Ethnicity	Black	8014.12	26174.0	(18.5, 153180.3)	2.2E+09	1.3E+10	(0, 8.1E+10)
	Native Am	19	0	(19, 19)	0	0.0E+00	(0, 0)
	White	13372.67	40057.6	(14.6, 242520)	1.8E+09	9.4E+09	(0, 8.3E+10)
	Latino	4217.2	10186.2	(19, 25009.5)	2.1E+08	5.1E+08	(0, 1.2E+09)
	Other	19	0	(19, 19)	0	0.0E+00	(0, 0)
Location	Both	29271.64	56615.6	(19, 185699.7)	1.1E+10	2.8E+10	(0, 8.3E+10)
	Knox	5441.24	17044.0	(16.9, 89906)	3.8E+08	2.0E+09	(0, 1.5E+10)
	Out	13919.66	44440.2	(14.6, 242520)	9.4E+08	3.2E+09	(0, 1.7E+10)

(+ values to the placement value)

Table 2. CD4 parameters

Factor	Response	mean CD4 count	CD4 count SD	CD4 count range	CD4 count variation	CD4 count variation SD	CD4 variation range
mental health trt	No	651.15	290.3	(168.4, 1390.2)	2.3E+04	3.1E+04	(0, 1.1E+05)
	Yes	668.61	321.6	(1, 1806.5)	5.4E+04	1.7E+05	(0, 1.2E+06)
Alcohol abuse hist.	No	666.08	305.6	(1, 1806.5)	4.9E+04	1.3E+05	(0, 1.2E+06)
	Yes	653.35	324.5	(90, 1488)	2.8E+04	3.4E+04	(0, 1.1E+05)
Drug abuse hist.	No	638.4	305.3	(1, 1806.5)	3.8E+04	1.3E+05	(0, 1.2E+06)
	Yes	727.2	317.3	(158.8, 1488)	5.6E+04	1.5E+05	(0, 9.3E+05)
IV drug abuse hist.	No	654.22	308.1	(1, 1806.5)	4.4E+04	1.5E+05	(0, 1.2E+06)
	Yes	722.56	326.8	(256.8, 1488)	3.4E+04	3.1E+04	(0, 1.1E+05)
Chronic Health iss.	No	666.9	302.8	(1, 1417.2)	2.7E+04	4.7E+04	(0, 2.9E+05)
	Yes	659.67	316.1	(90, 1806.5)	5.3E+04	1.7E+05	(0, 1.2E+06)
Chronic Pain iss.	No	663.02	318.3	(1, 1806.5)	3.7E+04	1.3E+05	(0, 1.1E+06)
	Yes	660.99	291.9	(158.8, 1251.7)	5.9E+04	1.6E+05	(0,9.3E+05)
Ethnicity	Black	617.33	339.5	(1, 1806.5)	2.2E+04	3.1E+04	(0, 1.3E+05)
	Native Am	487.38	0	(487.4, 487.4)	1.2E+04	0.0E+00	(1.2E+04, 1.2E+04)
	White	678.63	289.2	(90, 1488)	4.1E+04	1.2E+05	(0, 9.3E+05
	Latino	737.31	426.8	(147, 1313)	2.3E+05	4.8E+05	(2, 1.2E+06)
	Other	877.8	0	(877.8, 877.8)	2.6E+04	0.0E+00	(2.6E+04, 2.6E+04)
Location	Both	625.45	263.9	(224.1, 1313)	2.4E+04	1.5E+04	(867, 5.1E+04)
	Knox	680.9	304.5	(1, 1806.5)	6.6E+04	1.9E+05	(0, 1.2E+06)
	Out	648.47	344.1	(90, 1488)	2.1E+04	4.6E+04	(0, 2.9E+05)

Table 3. Multiple Regression results of individual factors



Multiple regression results for four models that explored the mean and variation in viral load and mean and variation in CD4 as explained by physical health (green), mental health (blue), demographic issues (orange), and substance abuse history (yellow). Any box that is filled in (black, gray, red) indicates a significant relationship with univariate ANOVA model. Light gray boxes indicate that factors were included within initial multiple regression however factors were not retained in the final averaged model of all models within 4 AIC units. Dark Gray boxes indicate factors that were retained within the final averaged model, had a positive relationship with response variable, however, were non-significant within the final model. Light red boxes indicate factors that were retained within the final averaged model, had a negative relationship with response variable, however were non-significant within the final model. Black boxes indicate a significant, positive relationship of the explanatory variable with the response variable, with * = $p < 0.05$, ** = $p < 0.01$. Dark red boxes indicate a significant, negative relationship of the explanatory variable with the response variable, with * = $p < 0.05$, ** = $p < 0.01$.

Table 4. Model parameters.for multiple regression

Response	*Predictor Variable*	*Estimate*	*Std. Error*	*P-value*
Mean viral load	**Live b/w rural & urban**	**7.0501425**	**1.96060440**	**0.0005**
Mean viral load	**Past memory issue**	**4.8849960**	**1.75056594**	**0.0061**
Mean viral load	**Non-denomination**	**6.6384810**	**2.97822679**	**0.0276**
Mean viral load	Substance abuse tx	2.1826534	1.36159896	0.1114
Mean viral load	Reside rural	-0.9726875	1.38395453	0.4835
Variance viral load	**Live b/w rural & urban**	**7.4689528**	**2.67573836**	**0.0061**
Variance viral load	**Non-denominational**	**9.3748554**	**4.05817467**	**0.0225**
Variance viral load	**Substance abuse tx**	**3.9833539**	**1.84685483**	**0.0329**
Variance viral load	**Christian faith**	**3.7086431**	**1.78788246**	**0.0401**
Variance viral load	Past memory issue	6.2539479	4.92957287	0.2069
Variance viral load	Reside rural	0.7206590	1.86574004	0.7000
Mean CD4 level	**Mean viral load**	**0.3682174**	**0.07218774**	**< 0.0001**
Mean CD4 level	**Substance abuse tx**	**2.4188310**	**1.16011672**	**0.0390**
Variance CD4 level	**Variance in viral load**	**0.1995118**	**0.06571761**	**0.0029**
Variance CD4 level	**Substance abuse tx**	**3.9553556**	**1.42985460**	**0.0065**
Variance CD4 level	Live b/w rural & urban	2.1640022	2.07504205	0.2990
Variance CD4 level	Past memory issue	3.4227390	3.75870554	0.3642
Variance CD4 level	Reside rural	0.1474864	1.40334485	0.9165

Significant values in bold

Table 5. Paths not included in SEM model

Missing Path	*Estimate*	*Std. Error*	*Df*	*Crit Value*	*P-value*
Mean CD4 level ~ Subst. Abuse Trt	1.0651	1.2366	128	0.8613	0.3907
Mean viral ~ Chronic Heath issue	0.5897	1.3416	125	0.4395	0.6610
Variance viral ~ Chronic Heath iss	-0.3115	1.5520	123	-0.2007	0.8413
Mean CD4 level ~ Chronic Heath iss	-0.0025	0.1373	128	-0.0181	0.9856
Variance CD4 ~ Chronic Heath iss	0.0871	0.8084	125	0.1077	0.9144
Variance viral ~ Past memory iss	3.1898	2.4066	124	1.3254	0.1875
Mean CD4 level ~ Past memory iss	-0.4746	1.5653	128	-0.3032	0.7622
Variance CD4~ Past memory issue	-0.4498	1.8483	125	-0.2433	0.8081
Mean CD4 level ~ Christian faith	-0.1461	1.1695	128	-0.1249	0.9008
Mean viral ~ Christian faith	1.8611	1.3058	125	1.4252	0.1566
Variance CD4~ Christian faith	1.0763	1.3743	125	0.7831	0.4350
Mean CD4 level ~ location	-0.2644	1.2114	127	-0.2182	0.8276
Mean viral ~ memory issues	5.0637	3.6418	125	1.3904	0.1669
Mean CD4 level~ memory issues	0.3693	3.2568	128	0.1134	0.9099
Variance CD4 ~ Non-denomination	2.5542	3.1313	125	0.8157	0.4162
Mean CD4 level ~ Non-denomin	0.6472	2.7216	128	0.2378	0.8124
Mean viral ~ Subs. Abuse Tx	1.0055	1.3251	125	0.7588	0.4494
Variance viral ~ Subst. Abuse Tx	1.5616	1.7959	124	0.8695	0.3862
Mean CD4 level ~ Subst. Abuse Tx	2.0689	1.3501	125	1.5324	0.1280
Mean viral ~ Ethnicity	-3.4088	7.2797	122	-0.4683	0.6404
Variance viral ~ Ethnicity	-6.0788	9.8690	121	-0.6159	0.5391
Mean CD4 level ~ Ethnicity	-2.1594	6.4520	125	-0.3347	0.7384
Variance CD4 ~ Ethnicity	-1.2567	7.5268	122	-0.1670	0.8677

Table 6. Variation explained by each model in SEM

Response Variable	*N*	R^2
Mean Viral Load	132	0.195
Variance in Viral Load	132	0.153
Mean CD4 Level	132	0.206
Variance in CD4 Level	132	0.172

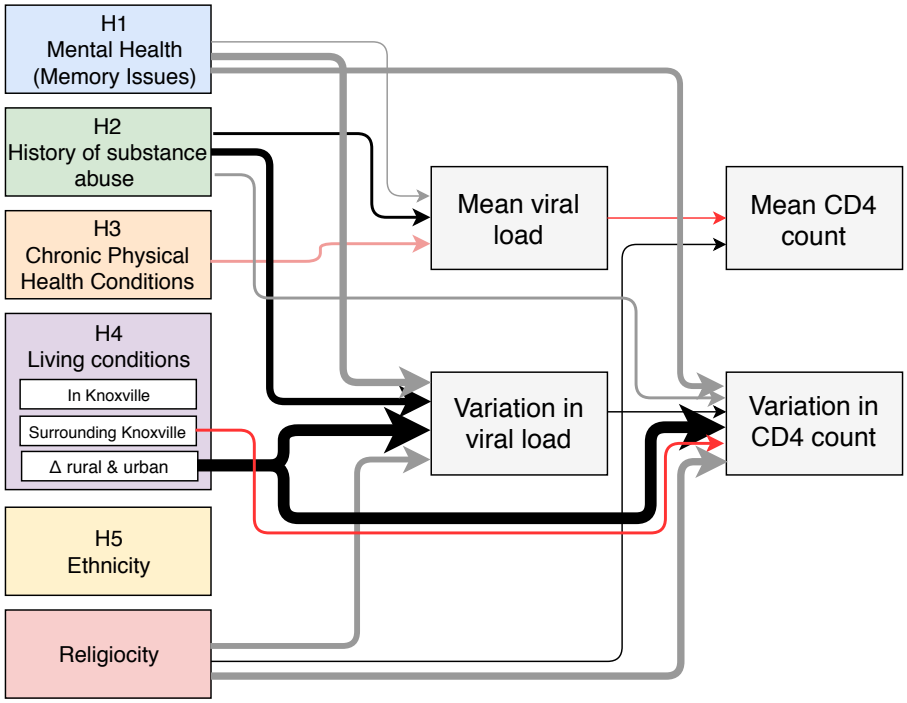


Figure 2. Structural Equation Model (SEM)

Line width drawn to weight – the thicker the line, the stronger the relationship. Black – significant positive relationship; Red – significant negative relationship; Grey – non-significant positive relationship; Pink – non-significant negative relationship

Vita

Shannon Bierma attended the University of Tennessee for her doctoral program in clinical psychology under the advisement of Dr. Todd Moore. Her research is in intimacy, sexual and gender identity development, clinical scale development, and HIV care. She volunteered with several advocacy groups, and worked to gain greater resources for the gay community in the region and fought legislation that discriminated against the community. She currently interns at Louisiana State University Medical School; working with psychosis, mood disorders, substance abuse disorders, trauma, neuropsychological assessment, and HIV care.