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Psychosocial Predictors of Depression and Medication Adherence in People Living with HIV

Sarah M. Henry
University of Miami, shenry@psy.miami.edu

UNIVERSITY OF MIAMI

PSYCHOSOCIAL PREDICTORS OF DEPRESSION AND MEDICATION ADHERENCE IN PEOPLE LIVING WITH HIV

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Sarah M. Henry

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Approved:

_____ Gail Ironson, Ph.D. Professor of Psychology	_____ Rick Stuetzle, Ph.D. Lecturer of Psychology
_____ Neil Schneiderman, Ph.D. Professor of Psychology	_____ Ray Winters, Ph.D. Professor of Psychology
_____ Julie Barosso, Ph.D. Professor of Nursing	_____ Guillermo Prado, Ph.D. Dean of the Graduate School
_____ David Kling, Ph.D. Professor of Religious Studies	

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INTRODUCTION: Depression is common in people living with HIV (PLWH) and is a primary predictor of poor adherence to HAART medications which brings serious health consequences. PLWH also tend to experience more stress and trauma in their lifetime, all of which have been implicated in the onset and exacerbation of depression and poor health behavior performance. Positive and negative psychosocial variables and coping strategies have been associated with psychosocial functioning and health behaviors suggesting that understanding the ways in which PLWH cope is key to understanding depression and health behavior performance within this population. Different coping techniques work differently depending on gender and more research is needed to clarify which coping strategies work best for which gender. Additionally, despite the frequency with which HIV and depression co-occur, there is little research investigating factors that predict the onset of depression in this population. Lastly, the impact of medication adherence on depression represents a gap in the literature.

OBJECTIVE: For the study detailed in this dissertation, we investigated the impact of nine different psychosocial variables and coping strategies on depressive symptoms and medication adherence. Additionally, we investigated how gender moderated these relationships. Lastly, we investigated the impact of medication adherence on depressive symptoms over time.

METHODS: A total of 177 HIV positive participants were asked to fill out self-report measures assessing a variety of psychosocial factors potentially related to disease progression and quality of life with HIV. Follow-up assessments were conducted at six month intervals for 2 years. Measures included psychosocial variables (optimism, social support, coping, benefit finding, stressful life events, and perceived stress), depressive symptoms, and medication adherence. Linear regression and hierarchical linear modeling were used to investigate cross-sectional and longitudinal relationships respectively.

RESULTS: Depressive symptoms were correlated with all positive and negative psychosocial variables with the exception of benefit finding. Gender moderated the relationship between adaptive coping and depressive symptoms. Religious coping and poorer medication adherence significantly correlated with fewer depressive symptoms for men only. Optimism, social support, avoidance coping, alcohol use, and perceived stress partially mediated the relationship between negative life events and depressive symptoms. Sub-optimal adherence predicted greater depressive symptoms in men only. Alcohol use predicted greater depressive symptoms over time for women only.

Positive psychosocial variables were not correlated with medication adherence. Optimism predicted better adherence while avoidance coping, perceived stress, depressive symptoms, and negative life events predicted poorer adherence. Gender moderated the relationship between negative life events and medication adherence. Negative life events significantly predicted poor adherence in women. Perceived stress correlated with poorer adherence in men only but was predictive of poor adherence for women only. Depressive symptoms significantly predicted poor adherence for both genders.

CONCLUSIONS: Positive and negative psychosocial variables have greater predictive power with more instrumental activities such as medication adherence than for depressive symptoms but correlate more strongly with depressive symptoms in PLWH. Additionally, different psychosocial variables correlate with and predict both depressive symptoms and medication adherence differently depending on gender of PLWH. Lastly, those psychosocial variables traditionally associated poor medication adherence seem to impact depressive symptoms in men and are predictive of greater depressive symptoms in men over time.

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Chapter 1: Introduction

Statement of the Problem

Human Immunodeficiency Virus (HIV) is considered a leading global health concern and affects more than 30 million people worldwide. In the United States alone, approximately 1.1 million people are living with HIV (PLWH) with an estimated 53,000 new infections occurring annually (UN AIDS Epidemic update, 2009). With the introduction of highly active antiretroviral treatment (HAART) in 1996, life expectancy for those living with the disease has increased from approximately 12 years from the time of infection (Barnett & Whiteside, 2006) to 20 years or more, especially if medication regimens are adhered to rigorously and health care recommendations are closely followed (Cooper, 2008). Therefore, as a result, HIV now meets criteria for a chronic illness as opposed to the acute infection it once was (Mahungu, Rodger, & Johnson, 2009).

As people live longer with HIV, the scope of health concerns affecting this particular population has expanded to include comorbid diseases and disorders, both physical and psychological. One of the most common comorbidities in PLWH is depression with estimates of prevalence rates ranging from 5% to as high as 48% (Evans, et al., 2005; Lyketsos & Federman, 1995), a rate much higher than seen in the general population. Depression is of particular concern in PLWH as it has been identified as a major contributor to all-cause mortality as well as disease progression (Lima, et al., 2007; Ironson, et al., 2005; Leserman, 2008) and has been cited as the leading factor in poor medication adherence (Starace, 2002; Ammassari, et al., 2004). It has also been associated with numerous transmission risk behaviors (Bing, et al., 2001; Brown, et al., 2006) significant decreases in well-being, and greater health care utilization (Baum, et al.,

2008). In short, depression is associated with not only problematic disease outcomes but also with problematic behaviors and problematic societal and financial burden.

Despite the vast amount of available literature about those factors associated with depression in PLWH, research prospectively examining factors associated with the occurrence of depression in this population is sparse and largely focuses on demographic or socioeconomic correlates of depression. Prospective research investigating factors more amenable to intervention, such as coping methods, could be particularly helpful with prevention, early identification, and early intervention with depression. Understanding such factors may have the potential outcome of avoiding the deleterious effects of depression on this particularly vulnerable population. Prospective research of this kind could also help identify those factors associated with the remittance of depression in PLWH. It is the intention of this study to identify and investigate those psychosocial factors associated with the development or remittance of depression.

Review of the Literature

Depression Prevalence in HIV

Although previous research has established that there is a high rate of depression in PLWH, the understanding of how these two factors are related remains unclear. For starters, the prevalence rates of depression among PLWH vary from study to study, as do the methods used to assess depression. There is some evidence suggesting that heterogeneity in measurement selection may partially be responsible for the differences in prevalence rates as self-report questionnaires (i.e. Center for Epidemiological Studies – Depression scale) tend to result in higher depression rates than interview-based

assessments such as the Structured Clinical Interview for the DSM-IV-TR (Sherr, et al., 2011).

In addition, it is unclear whether having HIV makes one more prone to depression or whether depression and HIV tend to occur within overlapping populations matched on relevant demographic characteristics. For example, Perkins, et al., (1994) reported no difference in depression, depressive symptoms, or depressive symptom severity between HIV+ and HIV- individuals from similar communities, though this study has been criticized for lack of sufficient statistical power (Ciesla & Roberts, 2001). In contrast, a meta-analysis of 10 studies conducted between 1988 and 1998 revealed that PLWH were twice as likely as HIV- matched controls to have had a recent depressive episode (Ciesla & Roberts, 2001). Both of these studies, however, predominately occurred prior to the widespread use of HAART which has had a significant impact on both lifestyle and longevity of PLWH and therefore may have also had an impact on depression within this population. Studies conducted within the post-HAART era still place the prevalence of depression in PLWH at approximately 2 to 9 times that of the general population (Pence, 2009). It is not surprising that the introduction of HAART has had little to no impact on depression prevalence in PLWH given that adherence to HAART regimens has been cited as a source of increased emotional distress (Lightfoot, et al., 2005; Siegel & Schrimshaw, 2005).

The Impact of Depression in HIV

Depression has been consistently associated with disease progression and poor physical health outcomes in PLWH. Along with faster progression to AIDS and increased

mortality risk (Ickovics, et al., 2001; Page-Shafer, et al., 1996; Patterson, et al., 1996), depression has been related to declines in CD8+ cells and NK cells (Leserman et al., 1997), both of which play pivotal roles in the suppression of viral replication. Depression has also been related to increased levels of HIV-related fatigue (Breitbart, et al., 2001) and strongly predicts decreased quality of life (Kemppainen, 2001).

Depression is of such concern in PLWH because of the strong association it has with high transmission risk behaviors and poor psychosocial functioning. Specifically, depression in PLWH has been related to engagement in risky sexual behavior and substance use, both of which are associated with disease progression and high disease transmission risk (Marks, Crepaz, & Janssen, 2006; O'Leary, et al., 2005). Also, smoking has been associated with depression in PLWH (Vidrine, Arduino, & Gritz, 2006). Other factors such as low striving for spiritual growth (Perez, et al., 2009), low social support, anhedonia, social and vocational impairment, and maladaptive coping have been associated with depression as well (Rabkin, 2008). Depression has also been consistently implicated in decreased adherence to HAART medications (Starace, et al., 2002).

Gender and Depression Prevalence in HIV

In the general population, women are diagnosed with depression approximately twice as often as men if not more (NIMH, 2008). It has been suggested that this pattern continues in PLWH; however, just as overall prevalence rates are somewhat unclear, prevalence rates of depression by gender are unclear as well. Given that women are accounting for a larger and larger percentage of new infections (26% of all diagnoses in

the U.S. in 2005; CDC, 2005), it is becoming increasingly more important to understand how gender influences depressive disorders in PLWH.

There is conflicting evidence for gender differences in depressive disorders such that some studies reporting as much as twice the incidence in women living with HIV (WLWH) than their male counterparts (Evans, Ten Have, & Douglas, 2002; Turner, et al., 2003) while others report no significant difference (Olley, et al., 2004; Haug, et al., 2005). Psychiatric co-morbidity, however, is more common in women living with HIV (WLWH) than men living with HIV (MLWH) (Haug, et al., 2005) and bereaved WLWH are more likely to meet diagnostic criteria for a psychiatric disorder than bereaved MLWH (Summers, et al., 2004). No gender differences have been reported for symptom severity in depressive disorders (Sledjeski, et al., 2005). Thus, the role gender plays in not only the incidence of but also the course of depressive disorders in PLWH remains unclear.

Stress in HIV

The fact that PLWH have a higher prevalence of depression than the general population is hardly surprising given the significant amount of stress they face daily and the high prevalence of lifetime traumatic experiences they report. Stressors for PLWH not only surround the disease itself but also stem from life circumstances often associated with having and managing HIV. Common psychosocial stressors in this population include coping with the internalized and experienced stigma of HIV, reformulating one's self-identity to incorporate the illness, fear of social and romantic rejection, and bereavement over friends and loved ones lost to AIDS. Common stressors specifically

associated with the disease itself include having to self-manage the illness (e.g. following medication regimens, making lifestyle changes, maintaining lifestyle changes, etc.) and subsequent medication side effects. PLWH also have to manage emotional reactions to the uncertainty regarding disease course and progression inherent in HIV/AIDS (Ironson & Kremer, 2010; Seigel & Lekas, 2002; Mercier, Reidy, & Maheu, 1999).

Stressful Life Events and Trauma in HIV

In addition to the burden of numerous daily stressors, PLWH often present with complicated psychosocial histories that frequently involve at least one traumatic experience or significantly stressful life event outside of receiving the HIV diagnosis itself (considered a significantly stressful life event). In a large study of PLWH in several southern states, 50% of participants reported a history of either physical or sexual abuse. 30% of males and 38% of females reported lifetime sexual abuse with approximately 25% of all participants reporting the sexual abuse having occurred before the age of 13 (Whetten, et al., 2006). Sexual and physical abuse continue to be common in this population even after an HIV diagnosis; 14% of PLWH reported experiencing physical abuse within the past 6 months while 6% reported having experienced sexual abuse within the same timeframe (Sowell, et al., 1999). Domestic violence is also remarkably common, especially among women living with HIV (Zierler, et al., 2000).

The Impact of Stress, Stressful Life Events, and Trauma in HIV

The impact of stress and trauma on PLWH is noteworthy. Not only are stressful life events associated with poor psychosocial functioning in PLWH, research has also demonstrated that stress and traumatic experiences contribute to faster disease progression (Ironson, et al., 2005). The relationship between stress, traumatic experiences, and disease progression is potentially dose-dependent such that the greater the number of traumatic experiences one has survived or the more stress one experiences within their lifetime (either via stressful life events or cumulative stress), the risk of developing AIDS doubles while the risk of developing a category C symptoms triples (Leserman, et al., 2002). It is possible that the relationship between stress and disease progression is mediated by medication adherence as increased levels of stress have been related to poor medication adherence (Leserman, Ironson, et al., 2006) which itself can result in faster disease progression and increased transmission risk (Balfour, et al., 2006; Quinn, et al., 2000). Further research is needed to clarify the mechanistic relationship between these three variables.

Gender and Stress, Stressful Life Events, and Trauma in HIV

WLWH face a unique set of additional stressors (Mello, Segurado, & Malbergier, 2010) associated both with the physical disease itself as well as stressors secondary to or outside of HIV. Some stressors specifically associated with the disease are gynecological side effects such as amenorrhea, cervical dysplasia, increased risk of cervical cancer with comorbid human papilloma virus (HPV) and HIV infection, and increased frequency of vaginal candidiasis (Semple, et al., 2003). Other stressors uniquely faced by women

include those associated with being and HIV positive mother such as disclosing serostatus to children or worrying about disease transmission en utero (Semple, et al., 2003). Women also report greater feelings of isolation, stigma, shame, and anxiety related to their serostatus compared to their male counterparts (Chung & Magraw, 1992). These psychosocial stressors have been shown to be as important in the development of depressive disorders for women as the physical burden of managing HIV (McIntosh & Rosselli, 2012).

Although no known report specifically addressed gender differences in stressful life events in PLWH, WLWH are more likely than men to report traumatic events and subsequent symptoms consistent with Posttraumatic Stress Disorder (Olley, et al., 2004). To elaborate, WLWH report higher rates of sexual assault after the age of 15 which is associated with increased risk for mental illness, high-risk behavior such as needle-sharing and unprotected sex, increased alcohol use, and decreased quality of life (Whetten, et al., 2008). They are also more likely to be in current abusive relationships (Zierler, et al., 2000) and therefore at may be at greater risk for experiencing further trauma.

Importance of Coping in HIV

Despite the widespread use and availability of HAART medications, having and managing HIV is often considered demanding and stressful by those carrying the illness (Ramien, et al., 2006). As mentioned above, stress and trauma outside of the illness are also prevalent among PLWH. To compound the issue further, stress, trauma, and stressful life events have been consistently implicated in the onset and exacerbation of major

depressive disorders and symptoms (Kendler, Karkowski, & Prescott, 1999; Rayburn, et al., 2005) in both the general populace and in PLWH. Given that stress and depression have such a negative impact on this particularly vulnerable population, it is important to thoroughly understand the mechanisms by which such precipitating factors impact health and well-being (including mental health). These mechanisms are termed coping styles, and coping is defined as those "thoughts and behaviors that people use to deal with the internal and external demands of situations that are appraised as stressful" (Folkman & Moskowitz, 2004).

Coping has been a primary focus in HIV-related research and is considered to be a possible pathway via which the stressors impact health and well-being in PLWH. Coping styles can also be taught and therefore coping represents a possible point of intervention whereby cognitive and behavioral modifications can impact the long term health and well-being of PLWH. The literature on coping, however, is as heterogeneous as the depression literature, and for many of the same reasons. There is no one standard assessment for coping and therefore methods of assessing coping in PLWH vary widely. In addition, the types of coping studied also vary. Despite the heterogeneity in both types of coping and methods of measurement, most coping research is rooted in the theoretical framework as presented by the transactional model of stress and coping as presented by Lazarus & Folkman in 1984.

Models of Coping

Lazarus and Folkman theorized that the environment and the individual are constantly interacting with one another, meaning that the individual's interpretation of the

environment influences their thoughts, behaviors, and actions, which in turn exerts influence over the environment, and thus resembles a transaction between the two. When the individual interprets the environment as threatening or stressful, subsequent thoughts and behaviors will automatically be aimed at reducing, escaping, or resolving that threat. These behaviors, thoughts, and actions are efforts to cope with the threat or stressor. For a situation to be considered stressful to the individual, it must represent some kind of threat or potential harm to something deemed important or significant (Pargament, 1997).

The process of interpreting the environment as threatening or stressful and assessing what contributed to the situation is termed the "primary appraisal". The primary appraisal is defined as "evaluations of life events in terms of their implications for the individual's well-being" (Pargament, 1997; Lazarus & Folkman, 1984). Following the primary appraisal is the secondary appraisal, where the individual assesses what resources and strengths he has available to him with which to combat the threat or stressor. Just how stressful a situation is considered to be results from a combination of the primary and secondary appraisal: the more a situation is interpreted as threatening to something meaningful to the person and the fewer the resources perceived to be available with which to handle the stressor, the greater the level of stress.

Though the transactional model of stress and coping serves as a foundation for understanding the coping process, other models that modify or add to it have been proposed. One such model is termed "the meaning-making model of stress and coping" (Park & Folkman, 1997). Though it retains the basic elements of the transactional model, this model elaborates on the way in which a person interprets a situation and their available resources. Park & Folkman theorize that people have a sense of "global

meaning", defined as "the most generalized and abstract level of meaning and contains a person's beliefs, expectations, goals, and fundamental assumptions about the world" (Park, 2005). Global meaning can be thought of as a lens through which one views the world that determines what is viewed as stressful and what resources are seen as available. Factors that potentially influence this "lens" include one's sense of spirituality and long-standing personality features such as optimism, making such factors potentially influential over the level of stress one experiences and the impact stress has on health and well-being.

Coping, Health, and Well-being in HIV

With depression, stress, stressful life events, and traumatic experiences all having been related to faster disease progression in PLWH, it's important to understand how coping may factor into the impact of such experiences. Slower disease progression has been associated with approach-oriented coping techniques such as maintaining a fighting spirit (Solano, et al., 1993), planful problem solving (Vassend & Eskild, 1998), optimistic outlook (Blomkvist et al., 1994), proactive behavior (Ironson, Balbin, et al., 2005), self-efficacy (Ironson, Weiss, et al., 2005), social support (Leserman, et al., 2002), and positive expectancies (Ickovics, et al., 2006). In addition, certain personality characteristics have also been associated with slowed disease progression, specifically consciousness, openness, and extroversion (Ironson, et al., 2008), as have increases in spirituality and the use of spirituality to cope with adversities (Simoni, et al., 2006; Ironson & Kremer, 2009).

In a recent meta-analysis on effective coping in PLWH (Moskowitz, et al., 2010), problem-focused coping techniques aimed at solving immediate, instrumental problems have been associated with increased quality of life, life satisfaction, and positive mood, less depression, emotional distress, perceived stress, and traumatization, and better health behaviors in the post-HAART era. Pre-HAART, problem-focused coping techniques were also associated with better health outcomes, slowed disease progression, and fewer somatic symptoms. Positive reappraisal, benefit finding, and using spirituality to cope were also associated with greater positive affect, decreased negative affect, and better physical health.

Many studies investigating relationships between coping and psychosocial and physical health outcomes have dichotomized coping into two broad categories which encompass several specific coping techniques. A common method divides coping into approach-oriented coping (including acceptance, problem-focused coping, action taking, and optimism) and avoidance coping (including denial, substance use, social isolation, and behavioral disengagement). Studies employing this method have found that approach-oriented coping has been associated with decreased depression, decreased emotional distress, and decreased perceived stress as well as increased quality of life, increased life satisfaction, and increased positive mood. Approach-oriented coping has also been related to better health behaviors in PLWH. Avoidance coping has been shown to have the exact opposite effects on all aforementioned outcomes.

There are some coping techniques that have a mixed impact on PLWH. For example, self-blame has been identified as a contributor to negative affect; however, it has also been found to improve health behaviors. There is also some evidence that using

broad groupings of coping obscures the impact of specific coping techniques that may differentially impact mental and physical health. To illustrate, both acceptance and confronting a stressor fall under the umbrella of approach-oriented coping. Confrontive coping, however, is related to increased negative affect while acceptance has been associated with decreased negative affect. Moskowitz, et al., (2010) encourage researchers to investigate ways in which specific coping techniques relate to positive outcomes instead of looking at broad categories.

Gender and Coping in HIV

Different coping techniques have been found to be more or less effective for PLWH depending on gender. In women, the use of distraction and positive growth have been related to decreased depression, while in men the absence of positive growth was related to increased depression (Vosvick, et al., 2010). In addition, more emotional expression was associated with increases in depression in men within the same study, while the use of emotional expression was associated with increased depression in women in another (Packenham & Rinaldis, 2001). Women tend to use spirituality as a way of coping more than men (Olley, et al., 2004; McIntosh & Rosselli, 2012). The use of alcohol, a common avoidance coping strategy, has been associated with increased depression in both men and women; however the strength of those relationships differs by gender across several studies (Olley, et al., 2004; Moskowitz, et al., 2010; McIntosh & Rosselli, 2012; Sherr, et al., 2011) with some reporting a stronger relationship for women and others finding a stronger relationship for men. Social support has also been related to better psychosocial functioning in both men and women, though it is often related to

better outcomes in women (Packenham & Rinaldis, 2001). A recent meta-analysis on stress and coping in WLWH, however, failed to find a relationship between social support and better mental health (McIntosh & Rosselli, 2012). In short, there is evidence suggesting coping techniques are more or less effective depending on gender; the evidence, however, is mixed and requires further investigation and clarification.

Adherence in HIV

Medication adherence has received a great deal of attention in HIV-related research, primarily because the rate of medication adherence is relatively low, and the potential impact of low medication adherence is significant not only for the individual but also for society. HAART medication regimens are usually demanding and require medicines to be taken at particular times of day under particular circumstances, such as with food or on an empty stomach. HAART medications also come with a plethora of unpleasant side effects, including nausea, fatigue, gastrointestinal upset, and lipodystrophy. To be effective, HAART regimens have to be taken with 90 to 95% accuracy, unlike most medication regimens which typically only require an 80% adherence rate for effectiveness. Consequences of adherence rates below 95% include increased disease progression, increased risk of disease mutation to a drug-resistant strain, and increased risk of transmission due to lack of viral load control. Disease mutation represents a particularly unfavorable outcome of suboptimal adherence; if the disease strain becomes drug resistant, there are no medication options with which to treat it.

Depression and Adherence in HIV

Because suboptimal medication adherence has such negative consequences, there have been great efforts to understand its primary correlates and contributors. As previously mentioned, depression has been identified as a primary predictor of suboptimal adherence in PLWH (Starace, 2002). Given that some symptoms of depression are confounded with symptoms of HIV, a closer look at the relationship between depression and adherence is necessary. Specifically, cognitive symptoms associated with depression such as decreased concentration and depressed mood have been more strongly related with lower adherence than somatic symptoms (Wagner, et al., 2011); however, fatigue, a common somatic symptom associated with depression, has been related to decreased adherence. In addition, depression severity also plays a role in adherence as severe depression has been more strongly correlated with lower adherence. Additional personal factors have been related to medication adherence as well, such as education (Martinez, et al., 2012), health care beliefs (Wendorf & Mosack, 2013), and complex psychosocial histories including PTSD, sexual and/or physical abuse histories (Whetten, et al., 2006).

Different coping methods have also been associated with differences in medication adherence. Specifically, self-efficacy has been identified as a major contributor to adherence in PLWH whereas escape-oriented coping strategies have been related to lower adherence (Deschamps, et al., 2004). Interestingly, planned problem-solving coping strategies were related to lower adherence in the same study despite similar coping strategies being related to better psychosocial functioning (Moskowitz, et

al., 2010). Perceived quality of social support and positive states of mind were also related to improved medication adherence (Gonzalez, et al., 2004).

Gender and Adherence in HIV

The literature has consistently found that WLWH are less adherent to medication regimens than men (Berg, et al., 2004). Men who start out with better health status maintain better adherence rates while women with poorer health status are more likely to be adherent than women with better initial health status. Widowed women tend to have better adherence than non-widowed women (Ortega, et al., 2012). Avoidance coping has been associated with decreased adherence in both men and women separately (Haukitis, et al., 2005; McIntosh & Rosselli, 2012) as has substance use though there is some evidence that different substances impact adherence in men and women differently (Berg, et al., 2004). Alcohol has been associated with decreased adherence in both men and women (Olley, et al., 2004; Berg, et al., 2004), though it is cited as a correlate of suboptimal adherence for men more often.

Directionality of Relationship between Depression and Medication Adherence in HIV

The directionality of the relationship between medication adherence and depression has yet to be fully understood. Most research relating the two has either just noted their cross-sectional correlation or has used depression as a predictor of lower medication adherence. There has yet to be a longitudinal investigation of the impact of medication adherence on depression but clarification regarding the directionality of this relationship has been identified as a gap in the literature (Gonzalez, et al., 2011), especially given research suggesting that HAART medications may negatively impact

levels of neurotransmitters in the brain known to contribute to depression (Zangerle, et al., 2002).

Summary

In summary, HIV continues to be a global health concern as millions are living with the disease worldwide and infection rates remain steady. The lifespan of those infected has increased considerably with the advent of HAART regimens, though these medications come with significant drawbacks such as undesirable side effects, difficult regimens, and severe consequences to suboptimal adherence. Despite the serious consequences, low adherence to medications continues to be a problem among PLWH and therefore has attracted significant amounts of research in effort to understand the barriers and impediments to adherence as well as the points for potential intervention to improve adherence.

Depression has been identified as a primary predictor of poor adherence to HAART medications in PLWH. Depression, however, does not only affect adherence in PLWH but also negatively impacts mortality, disease progression, health behaviors, and quality of life as well as increases health care utilization. Depression is the most common comorbidity in PLWH with estimates of its prevalence approximating twice that of the general population. Despite the frequency with which HIV and depression co-occur and the deleterious impact of depression on PLWH, there is a striking paucity of research investigating those factors that predict the onset of depression in this population.

Stress, stressful life events, and traumatic experiences have all been implicated in the onset and exacerbation of depression. Due to the complications surrounding living

with HIV, PLWH tend to have significantly more stressors to manage on a daily basis than the average individual. In addition, PLWH tend to have higher rates of stressful life events and are more likely to have at least one traumatic experience in their lifetime. Understanding the ways in which PLWH cope with such adversity is key to understanding depression and health behavior performance within this population.

Research investigating coping in HIV is varied and methodologies are heterogeneous making it difficult to synthesize findings for a harmonious understanding of the research. Despite this heterogeneity, different coping techniques have been differentially associated with psychosocial functioning, health outcomes, and health behaviors indicating that coping may be a potential mechanism by which stress impacts depression and disease processes. Coping also represents a potential point of intervention to improve or prevent decreased well-being, negative health behaviors, and declines in physical health. In addition, illuminating the ways in which long-standing coping techniques influence the impact of stressors and stressful life events on mental health has implications for possible interventions aimed at building resilience in this vulnerable population. Not all PLWH use similar coping strategies and different coping techniques work differently depending on several demographic grouping variables, particularly gender, though more research is needed to clarify of which coping strategies work best for which gender.

Understanding how depression and coping uniquely impact PLWH by gender is becoming increasingly important as infection rates for men and women globally are approaching equal and women comprise a larger and larger percentage of new infections each year. Gender uniquely impacts the relationship between disease progression,

mortality, health behaviors, and psychosocial well-being. There are also prevalence differences in depression by gender in PLWH as well as differences in barriers to and impediments of health behavior performance.

As noted above, the literature has established a significant and negative relationship between depression and medication adherence. The directionality of that relationship, however, remains obscure. Research has implicated depression as preceding suboptimal medication adherence; however, no research has investigated the impact of medication adherence on depression. Indeed, this has been identified as a significant gap in the literature as recent findings have suggested that HAART medications may alter neurochemistry in such a way that increases vulnerability for depression.

The primary aims for this study are to investigate those psychosocial factors predicting the onset, exacerbation, or remittance of depression in PLWH. Given that stress and stressful life events are so prevalent in PLWH, these factors will be investigated both directly and as buffers for the impact of stress on depression. In addition, medication adherence is of the utmost importance in PLWH and therefore we will also investigate factors predicting medication adherence in our sample. We will also examine how psychosocial factors buffer or accentuate the impact of stressful life events on medication adherence. Because our data is longitudinal, we are in a unique position to examine the directionality of the relationship between medication adherence and depression in PLWH and therefore will do so as it has been identified as a significant gap in the literature.

As gender becomes increasingly important in the HIV/AIDS epidemic, a thorough understanding of how gender uniquely influences stress, depression, and health behaviors

in PLWH is necessary. Our study aims to investigate how gender moderates all aforementioned relationships to shed light on the unique experiences of men and women living with HIV.

Chapter 2: Aims and Hypotheses

The main objective of this dissertation is to explore those psychosocial factors, both positive (including benefit finding, spirituality, adaptive coping, social support, and optimism) as well as negative (alcohol use, avoidance coping, perceived stress, and negative life events) and their relationship to depressive symptoms and medication adherence in an HIV positive population both cross-sectionally and over time. Gender will be analyzed as a potential moderator for all aforementioned relationships. Also, positive and negative psychosocial variables will be examined as possible mediators of the impact of stressful life events on depressive symptoms and medication adherence in effort to understand how specific psychosocial variables affect the outcomes of interest within a stress-diathesis model. Stressors will include those life events considered significantly stressful as measured by the Life Events Scale. Additionally, this dissertation seeks to understand the directionality of the relationship previously established by the literature between medication adherence and depression.

There are seven main hypotheses to be tested. 1) Positive psychosocial variables (benefit finding, spirituality, adaptive coping, social support, and optimism) will be correlated with fewer depressive symptoms and better medication adherence cross-sectionally and predictive of depression and medication adherence over time (see aims 1a and 3a). 2) Negative psychosocial variables (alcohol use, avoidance coping, perceived stress, and negative life events) will be correlated with more depression and worse medication adherence cross-sectionally and predictive of more depression and worse medication adherence over time (see aims 2a and 4a). 3) Gender will moderate the relationship between psychosocial variables and depressive symptoms both cross-

sectionally and longitudinally (see aims 1b and 2b). 4) Gender will moderate the relationship between both positive and negative psychosocial variables and medication adherence both cross-sectionally and longitudinally (see aims 3b and 4b). 5) Positive psychosocial variables will buffer the negative impact of stressful life events on depressive symptoms and medication adherence both cross-sectionally and over time while negative psychosocial variables will exacerbate the negative impact of stressful life events on depressive symptoms and medication adherence both cross-sectionally and over time (see aims 5 and 6). 6) Worse medication adherence will be predictive of the greater depressive symptoms over time (see aim 7a-7c).

Aim 1a: To determine whether positive psychosocial variables (benefit finding, spirituality, adaptive coping, social support, and optimism) will be correlated with depression cross-sectionally and will predict less depression over time

Aim 1b. To determine whether gender moderates the relationship between positive psychosocial variables and depression cross-sectionally and over time

Hypothesis 1a: Positive psychosocial variables will be correlated with less depression cross-sectionally and will predict less depression over time.

Hypothesis 1b: Positive psychosocial variables will be more strongly correlated with and predictive of less depression for women cross-sectionally and over time. The absence of positive psychosocial variables will be more strongly correlated with and predictive of greater depression in men cross-sectionally and over time.

Aim 2a: To determine whether negative psychosocial variables (alcohol use, avoidance coping, perceived stress, and negative life events) will be correlated with more depression cross-sectionally and over time

Aim 2b. To determine whether gender moderates the relationship between negative psychosocial variables and depression cross-sectionally and over time

Hypothesis 2a: Negative psychosocial variables are correlated with more depression cross-sectionally and predictive of more depression over time.

Hypothesis 2b: Negative psychosocial variables will be correlated with more depression in both men and women cross-sectionally and will predict more depression in both genders over time. Specifically, greater alcohol use will be more strongly correlated with depression in men cross-sectionally and will predict greater depression in men over time. Perceived stress and negative life events will be more strongly correlated with depression in women cross-sectionally and will predict more depression in women over time. Avoidance coping will be equally correlated with depression in both genders and will equally predict depression in men and women over time.

Aim 3a: To determine whether positive psychosocial variables (benefit finding, spirituality, adaptive coping, social support, and optimism) are related to better medication adherence cross-sectionally and over time

Aim 3b. To determine whether gender moderates the relationship between positive psychosocial variables and medication adherence cross-sectionally and over time

Hypothesis 3a: Positive psychosocial variables will be correlated with and predictive of better medication adherence cross-sectionally and over time.

Hypothesis 3b: Gender moderates the relationships between positive psychosocial variables and medication adherence both cross-sectionally and over time. Due to mixed findings in the literature, no specific a priori relationships can be hypothesized.

Aim 4a: To determine whether negative psychosocial variables (alcohol use, avoidance coping, perceived stress, and negative life events) are correlated with worse medication adherence cross-sectionally and predictive of worse medication adherence over time

Aim 4b. To determine whether gender moderates the relationship between negative psychosocial variables and medication adherence cross-sectionally and over time

Hypothesis 4a: Negative psychosocial variables are correlated with worse medication adherence cross-sectionally and over time.

Hypothesis 4b: Avoidance coping and perceived stress will be more strongly related to and predictive of worse medication adherence for women than men cross-sectionally and over time. Alcohol use will be more strongly related to and predictive of depression for men than women cross-sectionally and over time. Negative life events will be equally related to and predictive of depression for men and women cross-sectionally and over time.

Aim 5: To determine whether psychosocial variables (both positive and negative) mediate the relationship between stressful life events and depression both cross-sectionally and over time.

Hypothesis 5: Psychosocial variables mediate the relationship between stressful life events and depression both cross-sectionally and over time.

1. Stressful life events are correlated with depression cross-sectionally and over time
2. Stressful life events are correlated with psychosocial factors
3. Psychosocial variables are correlated with depression cross-sectionally over time
4. Stressful life events are related to depression after accounting for the effects of psychosocial variables

Aim 6: To determine whether psychosocial variables mediate the relationship between stressful life events and medication adherence both cross-sectionally and over time.

Hypothesis 6: Psychosocial variables mediate the relationship between stressful life events and medication adherence both cross-sectionally and over time.

1. Stressful life events are correlated with medication adherence
2. Stressful life events are correlated with psychosocial variables
3. Psychosocial variables are correlated with medication adherence both cross-sectionally and over time
4. Stressful life events are related to medication adherence after accounting for the effects of psychosocial variables

Aim 7a: To determine whether depression predicts medication adherence over time

Aim 7b: To determine whether medication adherence predicts depression over time.

Aim 7c: To determine whether gender moderates the relationship between medication adherence and depression cross-sectionally and over time.

Hypothesis 7a: Depression will predict less medication adherence over time

Hypothesis 7b: The predictive power of medication adherence for the development of depression cannot be determined from the literature a priori. See literature review for information regarding questions of directionality for the causal relationship between these two variables.

Hypothesis 7c: Sub-optimal medication adherence will predict more depression in women than men.

Chapter 3: Methods

Methods

Subjects

177 subjects were recruited to participate in a larger, longitudinal study on a voluntary basis in the south Florida area between 1997 and 2002. Demographic breakdown of subjects is as follows: 111 male, 66 female, 65 African-American, 53 Caucasian, 51 Hispanic, 89 self-identified gay men, 38 African-American women. Nine of 89 gay males also self-identified as African-American.

Subjects were asked to fill out self-report measures assessing a variety of psychosocial factors potentially related to disease progression and quality of life with HIV. Subjects also participated in individual interviews at each follow-up time point to further assess quality of life, stressful life events, and coping tools most useful for them.

Because participants were part of a larger parent study, inclusion/exclusion criteria, study design, study procedures, and psychometrics utilized have been published in Ironson, O'Cleirigh, et al., 2005. As such, the following description has been quoted from the aforementioned study. It should be noted that the data for this particular study covers only follow-up assessments through year 2 of the study.

As stated in Ironson, O'Cleirigh, et al., 2005:

> **Inclusion/exclusion criteria**
> Subjects were included in this study if they were HIV positive and had CD4 cells between 150 and 500 at study entry, thus capturing people in the midrange of disease who we hypothesized would be most vulnerable to the possible impact of psychosocial factors on HIV disease. Subjects were excluded if they had ever experienced an AIDS-defining (Category C) symptom, ever had CD4 cells below 75, were under age 18, had other life-threatening illnesses (e.g.,cancer), were

actively psychotic or suicidal, had dementia or current alcohol or drug dependence or current IV use

Design:
This study used a longitudinal design where participants were assessed every 6 months for a period of 2 years. The accrual period lasted 2.5 years, and the study period was from 1997 to 2002.
Procedures:
At baseline, subjects completed written informed consent, psychosocial questionnaires, a clinical assessment interview, and blood draw for CD4 and VL assay. Follow-up visits, repeated every 6 months, included the questionnaire battery, brief interview, and blood draw. Study procedures, including informed consent, were approved by the institutional review board.

Questionnaires & Measures

Demographic information, medical information, and information on psychosocial well-being was voluntarily collected from subjects using self-report questionnaires and interviews with research staff.

Adherence

Subjects were given the AIDS Clinical Trials Group (ACTG) Adherence Measure (Chesney et al., 2000) in effort to assess compliance with medication instructions and regimens. The ACTG has consistently demonstrated good reliability (Cronbach's $a>0.80$) and validity (Reynolds, et al., 2007). Included in the ACTG are questions regarding type of medication, quantity of missed medication doses over the previous four days, frequency with which medication was not taken as directed, and medication side effects occurring within the previous month. Adherence to medication was calculated as the proportion of missed doses to total doses for the three days prior to study follow-up. To reduce reporting error, only three of four days were included in the calculation.

Psychosocial Measures

Depression

The Beck Depression Inventory (BDI-I) is a self-report measure of depressive symptoms experienced within the past week. Its reliability (Pearson $r = 0.93$) and validity (Beck et al., 1961) have been consistently high. The questionnaire can be divided into two subscales, the somatic scale and the cognitive/affective scale, each measuring separate clusters of depressive symptoms. Analyses will be run with both the total score and with the cognitive/affective subscale alone to account for any possible confound between somatic depressive symptoms and HIV-related symptoms. The range of possible scores is 0-63 with scores from 0-13 indicating a minimal level of depressive symptomology, scores from 14-19 indicate a mild level of depressive symptomology, scores from 20-29 indicating moderate depressive symptomology, and 30-63 indicating severe depressive symptomology.

Social Support

The Enrichd Social Support Instrument (ESSI) is a 7-item, self-report measure that assesses four domains of social support including instrumental, emotional, information, and appraisal (Vaglio, et al., 2004). The ESSI has been found to have good internal consistency (Cronbach's $\alpha = 0.88$), excellent reproducibility (intra-class correlation coefficient of 0.94) with good concurrent and predictive validity. The ESSI also shows positive correlations with social functioning ($r = 0.20$), symptom improvement, and better general and disease-specific quality of life, demonstrating good convergent validity. The ESSI has a possible range of scores from 6 to 30 with higher scores indicating greater levels of social support.

Optimism

The Life Orientation Test - Revised (LOT-R) (Scheier, et al., 1994) was used to measure dispositional optimism and pessimism. The LOT-R has demonstrated good internal reliability (chronbach's alpha = 0.72), good test-retest reliability (r = 0.68 over a 4-week interval, r = 0.79 over 28-month interval), and good construct and convergent validity as the LOT-R has been significantly correlated with variables such as hopelessness and depression in the expected directions (Scheier, et al., 1994; Burke, et al., 2000). The LOT-R has a possible range of scores from 0-40 with higher scores indicating lower levels of optimism. For ease of interpretation, all results tables title LOT-R results as "Low Optimism" to clarify that higher scores indicate lower levels of optimism.

Coping and Religious/Spiritual Coping

The Brief Cope Inventory is based on the COPE inventory, a 60-item instrument that comprises 15 scales. The Brief COPE consists of 14 scales, two items per scale. Participants are asked to rate on a Likert scale of 1 (I haven't been doing this at all) to 4 (I've been doing this a lot) the degree to which statements about different coping methods apply to them. All scales have demonstrated acceptable internal reliability (Carver, 1997). Range of possible scores for each subscale ranges from 2-8 with 2 indicating no use of the coping method while 8 indicates the frequent presence of the coping method.

Stressful Life Events

The Life Experiences Survey (Sarason, Johnson, & Siegel, 1978) was used to assess the occurrence of major life events in participants' lives within the past 6 months. The instrument assesses the desirability of the event by asking whether it was perceived

as positive or negative and assessing the stress impact of the event (a Likert scale of 1 = not stressful, 5 = extremely stressful). The measure has shown acceptable test-retest reliability and good construct validity (Sarason, Johnson, & Siegel, 1978).

Perceived Stress

The PSS is a 10-item scale designed to measure the degree to which individuals appraise situations in their lives as stressful. PSS items were designed to measure how unpredictable, uncontrollable, and overloading individuals find their lives to be as these three issues have been identified as central to the appraisal of stress. Internal reliability (chronbach's alpha = 0.86) and test-retest reliability has been shown to be adequate. The PSS has been significantly correlated with self-reported negative affect and physical symptoms, demonstrating convergent validity. Possible scores range from 0 to 40 with higher scores indicating a greater degree of perceived stress.

Cross-sectional Analyses

Cross-sectional Main Effects Models

The proposed cross-sectional hypotheses will be analyzed using Linear Regression (LR) (Pedhazur, 1997). LR allows us to examine whether or not and the degree to which depressive symptoms are related to positive psychosocial variables (PPSV) or negative psychosocial variables (NPSV) cross-sectionally. The relationship between medication adherence and positive and negative psychosocial variables will also be examined. LR was chosen because the degree to which both depressive symptoms and medication adherence relate to PPSV and NPSV can be calculated and interpreted. LR also allows us to control for potentially influential demographic characteristics such as

such as age, gender, level of education, and ethnicity. For illustrative purposes, the predictor measure below is PPSV and the outcome measure is depressive symptoms. The LR models to be used for all other cross-sectional, main effect relationships proposed will use a similar model with the appropriate independent variable and dependent variable. Any differences that arise upon data analysis will be documented and adjusted for.

Proposed Regression Equations for Testing Relationships to Outcome Variables

$Y(\text{Depression})_i = a_i + \beta_1(\text{age})_i + \beta_2(\text{gender})_i + \beta_3(\text{ethnicity})_i + \beta_4(\text{education})_i + \beta_5(\text{PPSV})_i + e_i$

Where:
Y_i = Depressive symptoms for participant i
a_i = Mean of the dependent variable in the population in the absence of PPSV
β_{5i} = Regression coefficient representing the effect of PPSV on depressive symptoms for participant i
β_{1i}- β_{4i} = Effect of the a priori covariates on change in depressive symptoms
e_i = Error term for participant i

The test of significance of the β_5 coefficient determines whether PPSV is significantly related to depressive symptoms.

Cross-sectional Moderation Models

In order to test whether gender moderates the relationship between PPSV and depressive symptoms in PLWH, an interaction term of gender-by-PPSV is added to the equation. Moderation implies that the strength of the relationship between PPSV and depressive symptoms differs depending on participant gender. Moderation is implied when the coefficient for the interaction term is significant, indicating that the relationship between PPSV and depressive symptoms differs significantly between males and

females. It does not, however, indicate that the relationship between PPSV and depressive symptoms for males or the relationship between PPSV and depressive symptoms for females is significantly different from zero.

Two additional LR analyses are required to test whether the relationship between PPSV and depressive symptoms for men or for women is significantly different from zero. Because the moderation variable of interest is categorical, it will be dummy coded. If males are dummy coded to 0, the test of significance on the β_5 coefficient indicates the presence of an effect of PPSV on depressive symptoms for men. To test whether the effect of PPSV on depressive symptoms is significantly different from zero for women, gender must be recoded such that 0 = female and the regression must be repeated.

Proposed Regression Model for Testing Moderation

$Y(\text{depression})_i = a_i + \beta_1(\text{age})_i + \beta_2(\text{gender})_i + \beta_3(\text{ethnicity})_i + \beta_4(\text{education})_i + \beta_5(\text{PPSV}) + \beta_6(\text{PPSV*gender})$

Where:
Y_i = Depressive symptoms for participant i
a_i = Mean of the dependent variable in the population in the absence of PPSV
β_{5i} = Regression coefficient representing the effect of PPSV on depressive symptoms for participant *i* when gender is 0
β_{6i} = Regression coefficient representing the moderating effect gender the relationship between PPSV and depressive symptoms for participant *i*
β_{1i}- β_{4i} = Effect of the a priori covariates on change in depressive symptoms
e_i = Error term for participant i

Cross-sectional Mediation Models

In order to test whether negative life events (NLE) mediates the relationship between PPSV and depressive symptoms, PPSV and negative life events must first be significantly related to the outcome variable independently. Mediation by negative life events is signified if the relationship between PPSV and depressive symptoms is no

longer significant after adding negative life events into the model as a mediator but negative life events continue to be significantly related to depressive symptoms. All mediation models proposed will be tested using the same model as illustrated below. Any differences that arose upon data analysis were documented and adjusted for.

Proposed Regression Equations for Testing Mediation

$$Y(\text{depression})_i = a_i + \beta_1(\text{age})_i + \beta_2(\text{gender})_i + \beta_3(\text{ethnicity})_i + \beta_4(\text{education})_i + \beta_5(\text{PPSV})_i$$

$$Y(\text{depression})_i = a_i + \beta_1(\text{age})_i + \beta_2(\text{gender})_i + \beta_3(\text{ethnicity})_i + \beta_4(\text{education})_i + \beta_5(\text{NLE})_i$$

$$Y(\text{depression})_i = a_i + \beta_1(\text{age})_i + \beta_2(\text{gender})_i + \beta_3(\text{ethnicity})_i + \beta_4(\text{education})_i + \beta_5(\text{PPSV})_i + \beta_6(\text{NLE})_i + e_i$$

Longitudinal Analyses

The proposed longitudinal analyses will use Hierarchical Linear Modeling (HLM) (Bryk & Raudenbush, 2002; Raudenbush et al., 2002) to explore the associations between depressive symptoms, medication adherence, PPSV, and NPSV. Within these analyses, it was determined that PPSV and NPSV are related to depressive symptoms and medication adherence over time. HLM was chosen because it allowed for the prediction of the slope of depressive symptoms and medication adherence over time. HLM also allows us to control for potentially influential demographic characteristics that differ between individuals such as age, gender, ethnicity, and education. We also controlled for type of medication prescribed to account for any possible medication variance over time. Outcome measures were medication adherence and depressive symptoms.

With HLM, variance in outcome measures is separated into two levels. Variables that change at the level of the person (within subjects), such as amount of time between

assessments since baseline, type of HIV medication (no medication, combination therapy, or HAART), and the interaction between elapsed time and type of HIV medication are to be evaluated at the first level of analysis. We also include a variable that models the amount of time between assessments created the structure needed to model the slope and intercept.

Variables that change at the level of the group (between subjects), such as age, ethnicity, gender, and education level, are to be evaluated at the second level of analysis (coded 1 = male, 0 = female), race (coded 1 = non-Hispanic, Caucasian, 0 = other), and education (coded 0 = less than high school, 1 = some high school, 2 = high school graduate, 3 = trade-school or some college, 4 = college graduate, 5 = graduate degree).. These variables were chosen due to established research identifying these demographic characteristics as gold-standard covariates in HIV-related research. HIV often has a negative impact on employment due to illness complications and therefore also on income. We use education level as a measure for SES to account for this effect. Predictors are also included at the second level of analysis to determine the main effects of PPSV and NPSV on medication adherence and depressive symptoms over time. All continuous variables are centered and all categorical variables are dummy coded (with zero as the lowest level).

Proposed equations for analyses are below. The HML models described use medication adherence as the outcome variables for illustrative purposes. The HLM models to test whether PPSV and NPSV are related to depressive symptoms are predicted to be the same as the equations above for medication adherence. Any differences that arise upon data analysis will be documented and adjusted for.

Proposed HLM Equations for Testing Relationships to Outcome Variables

Level 1:

$Y_{ti} = \beta_{0i} + \beta_{1i}(\text{months since baseline})_{ti} + \beta_{2i}(\text{antretroviral1})_{ti} + \beta_{3i}(\text{antretroviral2})_{ti} + \beta_{4i}(\text{antretroviral1} \times \text{time})_{ti} + \beta_{5i}(\text{antretroviral2} \times \text{time})_{ti} + e_{ti}$

Where:

Y_{ti} = Medication adherence for participant i at time point t

β_{0i} = Medication adherence for the ith participant

β_{1i} = Slope representing change in medication adherence for participant i

β_{2i}, β_{3i}, β_{4i}, β_{5i} = Slopes for dummy coded HIV medication variables and the interaction of antiretroviral medications and months since baseline, allowing us to control for changes in medication adherence possibly resulting from differences in medication.

e_{ti} = Error term for participant i at time t

In order to examine individual differences in level 1 change parameters, level 2 equations are needed.

Level 2:

β_{01} (intercept) = $\gamma_{00+} + u_0$

β_{1i} (slope of medication adherence) = $\gamma_{10} + \gamma_{11}(\text{baseline medication adherence}) + \gamma_{12}(\text{age})_i + \gamma_{13}(\text{gender})_i + \gamma_{14}(\text{ethnicity})_i + \gamma_{15}(\text{education})_i + \gamma_{16}(\text{PPSV})_i + u_1$

$\beta_{2i,\ 3i} = \gamma_{20}, \gamma_{30}$ (antiretroviral 1 or 2),

$\beta_{4i,\ 5i} = \gamma_{40}, \gamma_{50}$ (antiretroviral 1 or 2 × time)

Where:

γ_{00} = Group average of medication adherence

γ_{10} = Average change in medication adherence each time point

γ_{20} and γ_{30} = Average effect on level of medication adherence across patients from antiretroviral 1 or 2

γ_{40} and γ_{50} = Average effect on change in medication adherence across patients from antiretroviral 1 or 2

γ_{11}–γ_{15} = Effect of the a priori covariates on change in medication adherence

γ_{16} = Effect of individual differences on medication adherence slope ($\gamma 10$) attributable to PPSV

u0, 1 = unexplained individual variance related to the estimation of the γ coefficients.

Proposed HLM Equations for Testing Moderation

In order to test whether gender moderates the relationship between PPSV and medication adherence in PLWH, an interaction term of gender-by-PPSV is added to the level 2 equation. Moderation implies that the strength of the relationship between PPSV and medication adherence differs depending on participant gender. Moderation is implied when the coefficient for the interaction term is significant, indicating that the relationship between PPSV and medication adherence differs significantly between males and females. It does not, however, indicate that the relationship between PPSV and depressive symptoms for males or the relationship between PPSV and medication adherence for females is significantly different from zero.

Two additional analyses are required to test whether the relationship between PPSV and medication adherence for men or for women is significantly different from zero. Because the moderation variable of interest is categorical, it will be dummy coded. If males are dummy coded to 0, the test of significance on the β_5 coefficient indicates the presence of an effect of PPSV on medication adherence for men. To test whether the effect of PPSV on medication adherence is significantly different from zero for women, gender must be recoded such that 0 = female and the regression must be repeated.

Moderation:

β_{1i} (slope of medication adherence) = γ_{10} + γ_{11} (baseline medication adherence)$_i$ + γ_{12} (age)$_i$ + γ_{13} (gender)$_i$ + γ_{14} (ethnicity)$_i$ + γ_{15} (education)$_i$ + γ_{16} (PPSV)$_i$ + γ_{17} (PPSV*gender) + u_1

Proposed HLM Equations for Testing Mediation

In order to examine whether PPSV mediate the relationship between NLE and medication adherence, PPSV had to first be significantly related to the medication adherence and NLE had to be related to medication adherence. Mediation by PPSV is indicated when the relationship between NLE and medication adherence weakens to non-significance when PPSV are added into the model.

Mediation:

β_{1i} (slope of medication adherence) = γ_{10} + γ_{11} (baseline medication adherence)$_i$ + γ_{12} (age)$_i$ + γ_{13} (gender)$_i$ + γ_{14} (ethnicity)$_i$ + γ_{15} (education)$_i$ + γ_{16} (PPSV)$_i$ + u_1

β_{1i} (slope of medication adherence) = γ_{10} + γ_{11} (baseline medication adherence)$_i$ + γ_{12} (age)$_i$ + γ_{13} (gender)$_i$ + γ_{14} (ethnicity)$_i$ + γ_{15} (education)$_i$ + γ_{16} (NLE)$_i$ + u_1

β_{1i} (slope of medication adherence) = γ_{10} + γ_{11} (baseline medication adherence)$_i$ + γ_{12} (age)$_i$ + γ_{13} (gender)$_i$ + γ_{14} (ethnicity)$_i$ + γ_{15} (education)$_i$ + γ_{16} (PPSV)$_i$ + γ_{17} (NLE)$_i$ + u_1

Mediation is established if NLE are no longer significantly related to medication adherence after adding PPSV to the equation, but PPSV remains significantly associated with medication adherence. All proposed longitudinal mediation models are expected to use the above model. Any differences that arose upon data analysis were documented and adjusted for.

Chapter 4: Results

Sample Characteristics

Participants (n = 177) came from a larger longitudinal study (Ironson, O'Cleirigh, et al., 2005). Demographic and medical information can be found in the aforementioned publication. Demographic information relevant to this particular study (gender, ethnicity, and education) is located in Table 1. At baseline, 77% of participants reported taking antiretroviral medications. At the two year follow-up, 90% of participants reported taking antiretroviral medications. Mean BDI-II scores and proportion of missed doses for antiretroviral medications for each time point can be found in Tables 2 and 3. Descriptive statistics for positive and negative psychosocial variables can be found in Table 4. Descriptive statistics for positive and negative psychosocial variables by gender can be found in tables 5 and 6. An independent samples t-test was conducted to compare scores on PPSV by gender. With the exception of religious coping (t = -2.484, p = 0.015), there were no significant gender differences in PPSV scores. These results can be found in table 7.

Testing of the hypotheses

The basic regression and hierarchical linear models used for all data analyses can be found in the "Methods" section on pages 28-39 accompanied by model equations and explanations.

Cross-sectional Relationship to Depression

Table 8 contains the significance tests for the cross-sectional relationship between positive and negative psychosocial variables and depressive symptoms. Covariates

significantly related to lower levels of depressive symptoms at baseline included higher education (β = -1.286, p = 0.003) and female gender (β = 0.174, p = 0.003). With the exception of benefit finding, all positive and negative psychosocial variables were significantly related to baseline depressive symptoms levels in the expected directions. Greater use of adaptive coping skills were significantly related to lower levels of depressive symptoms at baseline (β = -0.297, p <0.001). Higher levels of social support was significantly related to lower levels of baseline depressive symptoms (β = -0.422, p <0.001). Higher levels of pessimism were significantly related to higher levels of baseline depressive symptoms (β = 0.640, p <0.001). Greater use of religious coping was significantly related to lower levels of baseline depressive symptoms (β = -0.194, p =0.011). Greater use of maladaptive coping (reverse coded) was significantly related to higher levels of baseline depressive symptoms (β = -0.334, p <0.001). Greater alcohol use as a coping strategy (reverse coded) was significantly related to higher levels of baseline depressive symptoms (β = -0.347, p <0.001). Greater levels of perceived stress was significantly related to higher levels of depressive symptoms at baseline (β = 0.558, p <0.001). Higher levels of baseline depressive symptoms was also significantly related to having experienced a greater number of stressful life events within the past 6 months (β = 0.434, p <0.001). Lastly, a higher proportion of missed doses of antiretroviral medication over the previous 3 days was significantly related to higher levels of baseline depressive symptoms (β = 0.182, p =0.050).

Longitudinal prediction to Depression

Tables 10 and 11 contain the significance tests and results for the models used to predict change in depressive symptoms measured by slope while controlling for antiretroviral medications and time since baseline. Although there was not a significant change in depressive symptoms over time, there was significant individual variation in depressive symptoms over time (χ^2 (164) = 291.414, $p < .001$) which allowed for subsequent analyses. In contrast to the cross-sectional analyses, change in depressive symptoms over the 5 time points was not predicted by any of the positive or negative psychosocial variables while controlling for baseline depressive symptoms levels. Covariates that significantly predicted lower levels of depressive symptoms included male gender (γ_{13} = -0.1768, t (165) = -2.599, p = .010) and higher education (γ_{15} = -0.0386, t (165) = -1.987, p = .049).

Summary: Depression

The previously proposed hypotheses (see chapter 2: Aims and Hypotheses) find mixed support in the above findings. There was support for hypothesis 1a such that positive psychosocial variables are correlated with fewer depressive symptoms cross-sectionally with the exception of benefit finding, which was neither correlated with nor predictive of depressive symptoms. Additionally, the above findings support hypothesis 2a that negative psychosocial variables are correlated with more depressive symptoms cross-sectionally. Hypotheses 1b and 2b, however, did not find support as neither positive nor negative psychosocial variables were predictive of depressive symptoms over time. Lastly, medication adherence was not found to be a significant predictor of depressive symptoms over time (hypothesis 7a).

Cross-sectional Relationship to Depression Moderated by Gender

To test the hypothesis that gender moderates the cross-sectional relationship between positive and negative psychosocial variables and baseline depressive symptoms, a hierarchical multiple regression analysis was conducted. With the exception of medication adherence and benefit finding, all psychosocial variables accounted for a significant proportion of variance in baseline depressive symptom levels (see R^2 and *p* column in table 13). Prior to running the moderation analyses, all continuous variables and covariates were centered. An interaction term between all positive and negative psychosocial variables and gender was created (Aiken & West, 1991). The ΔR^2 column in table 13 represents the additional variance in baseline depressive symptoms accounted for by the interaction term between gender and PPSV. With the exception of adaptive coping ($\Delta R^2 = 0.032$, $\Delta F = 6.399$, $p = 0.012$), the interaction terms between gender and PPSV were not significant. In other words, save in the case of adaptive coping, the correlation between PPSV and baseline depressive symptoms did not significantly differ between men and women. The correlation between adaptive coping and baseline depressive symptoms did significantly differ between men and women ($t = -2.530$, $p = 0.012$). Use of adaptive coping was not significantly correlated with baseline depressive symptoms for women ($t = -0.292$, $p = 0.770$); however, greater use of adaptive coping was significantly related to lower levels of baseline depressive symptoms for men ($t = -4.877$, $p < 0.001$).

With the exception of religious coping, and medication adherence, the relationship between baseline depressive symptoms and all positive and negative

psychosocial variables significantly differed from zero for both men and for women. The relationship between baseline depressive symptoms and religious coping as well as the relationship between baseline depressive symptoms and medication adherence only significantly differed from zero for men such that a higher proportion of missed medication doses was significantly related to greater baseline depressive symptoms (t = 2.008, p =0.047) and greater use of religious coping was significantly related to fewer baseline depressive symptoms (t = -2.431, p =0.016). In contrast, medication adherence and religious coping did not account for any variance in baseline depressive symptoms for women.

Longitudinal Prediction to Depression Moderated by Gender

To test the hypothesis that the ability of PPSV to predict depressive symptoms over time differs depending on participant gender, three separate hierarchical linear modeling analyses were conducted for each independent variable. All analyses added an interaction term between gender and PPSV to the model and tested whether the prediction to depressive symptoms over time by each PPSV significantly differed between men and women. With the exception of medication adherence (γ_{17} = 0.6142, t (164) = 2.787, p = 0.006), gender did not moderate the prediction to depressive symptoms from baseline PPSV. After dummy coding males to 0, an additional regression analysis was performed and found that, for males, a higher proportion of missed medication doses (i.e. lower medication adherence) at baseline significantly predicted increased depressive symptoms over time (γ_{16} = -0.3502, t (164) = 2.219, p = 0.029). To test the same hypothesis for females, females were dummy coded to 0 and the regression

was repeated. Medication adherence at baseline did not significantly predict depressive symptoms levels over time for females (γ_{16} = -0.2640, t (164) = -1.694, p = 0.093). Substance use, however, did significantly predict depressive symptoms over time for females (γ_{16} = 0.0581, t (164) = 2.208, p = 0.029) such that greater levels of substance use at baseline significantly predicted an increased level of depressive symptoms over time. These results are summarized in tables 14 and 15.

Summary: Psychosocial Variables and Depression Moderated by Gender

The above findings do not support the hypothesis that positive psychosocial variables will be more strongly correlated with and predictive of fewer depressive symptoms for women cross-sectionally and over time (hypothesis 1b). Instead, the above findings suggest that the only correlation that differs depending on gender was that between adaptive coping and depressive symptoms. Greater use of adaptive coping was significantly correlated with fewer depressive symptoms for men only, and was unrelated for women. Interestingly, greater use of religion for coping was significantly correlated with fewer depressive symptoms in men but was not significantly related for women. Positive psychosocial variables did not significantly predict depressive symptoms over time for men or women.

The above findings do, however, support the hypothesis that negative psychosocial variables are correlated with more depressive symptoms in both men and women cross-sectionally and partially support the hypothesis that negative psychosocial variables predict more depressive symptoms over time in both men and women (hypothesis 2b). Specifically, although significant for both men and women, alcohol use

was more strongly correlated with depressive symptoms for men. Over time, however, alcohol use significantly predicted greater levels of depressive symptoms in women but not in men. Avoidance coping was equally correlated with more depressive symptoms for men and women. Avoidance coping, however, was not predictive of depressive symptoms over time for men or women. Although they were hypothesized to more strongly correlate with greater levels of depressive symptoms for women, perceived stress and negative life events were equally correlated with greater levels of depressive symptoms for men and women. Neither was predictive of depressive symptoms over time for either gender.

Contrary to what was hypothesized (hypothesis 7b), sub-optimal baseline medication adherence significantly predicted greater levels of depressive symptoms over time in men but was not a significant predictor of depressive symptoms over time for women.

Cross-sectional relationship between PPSV and Medication Adherence

Tables 16 and 17 contain the significance tests for the cross-sectional relationship between all positive and negative psychosocial variables and medication adherence. Education was the only covariate significantly related to medication adherence such that higher levels of completed education was significantly related to better medication adherence ($\beta = -0.271$, $p = 0.006$). With the exception of perceived stress and depressive symptoms, no PPSV were significantly related to medication adherence. Higher levels of baseline depressive symptoms were significantly related to greater proportion of missed medication doses (i.e. poorer medication adherence) ($\beta = 0.178$, $p = 0.050$). Similarly,

higher levels of perceived stress was significantly related to a greater proportion of missed medication doses ($\beta = 0.236$, $p = 0.008$).

Longitudinal prediction to Medication Adherence

Tables 18-19 contain the significance tests and results for the models used to predict change in medication adherence while controlling for antiretroviral medications and time since baseline. While there was not significant change in adherence over time, there was significant individual variation in medication adherence over time (χ^2 (137) = 160.81, $p = 0.030$). Change in medication adherence over the 5 time points was predicted by half (5 of 10) positive or negative psychosocial variables including optimism, maladaptive coping, perceived stress, depressive symptoms, and negative life events. Higher levels of pessimism at baseline significantly predicted a greater proportion of missed doses over time ($\gamma_{11} = 0.000311$, t (151) = 2.015, $p = 0.046$). Greater use of maladaptive coping at baseline significantly predicted a greater proportion of missed medication doses over time ($\gamma_{11} = -0.000883$, t (151) = -2.439, $p = 0.016$). Higher perceived stress ($\gamma_{11} = 0.000344$, t (151) = 3.794, $p < 0.001$) and higher depressive symptoms levels ($\gamma_{11} = 0.000344$, t (151) = 3.560, $p < 0.001$) at baseline significantly predicted greater proportion of missed medication doses over time. Lastly, a greater number of reported negative life events at baseline significantly predicted a greater proportion of missed medication doses over time ($\gamma_{11} = 0.001733$, t (151) = 2.843, $p = 0.005$). Covariates that significantly predicted better medication adherence included higher education ($\gamma_{15} = -0.0009$, t (151) = -1.943, $p = 0.05$).

Summary: Psychosocial Variables and Adherence

In general, the above findings did not support hypothesis 3a as positive psychosocial variables were neither significantly correlated with nor predictive of better medication adherence cross-sectionally or over time. Optimism, however, was the one exception such that lower levels of optimism significantly predicted worse medication adherence over time. Results partially support hypothesis 4a that negative psychosocial variables are correlated with worse medication adherence cross-sectionally and predominantly support the hypothesis that negative psychosocial variables predict worse medication adherence over time. Specifically, perceived stress and depressive symptoms were significantly correlated with and predictive of worse medication adherence. There was no significant correlation between medication adherence and avoidance coping or negative life events; however, both avoidance coping and negative life events were predictive of worse medication adherence over time. Alcohol use was neither correlated with nor predictive of medication adherence.

Cross-sectional Relationship to Medication Adherence Moderated by Gender

To test the hypothesis that gender moderates the cross-sectional relationship between positive and negative psychosocial variables and baseline medication adherence, a hierarchical multiple regression analysis was conducted. For further details regarding analysis, see section titled "Cross-sectional Relationship to Depression Moderated by Gender."

With the exception of negative life events ($\Delta R^2 = 0.031$, $\Delta F = 4.127$, $p = 0.044$), the interaction terms between gender and PPSV were not significant. This indicates that, save in the case of negative life events, the relationship between PPSV and baseline

medication adherence did not significantly differ between men and women. The relationship between negative life events and baseline medication adherence did significantly differ between men and women (t = 2.031, p = 0.044). A higher number of negative life events at baseline was not significantly related to baseline medication adherence for women (t = -0.610, p =0.543); however, a higher number of negative life events at baseline was significantly related to a greater proportion of missed medication doses for men (t = 2.591, p =0.011).

With the exception of perceived stress, the relationship between baseline medication adherence and all predictor variables did not significantly differ from zero for both men and women. The relationship between baseline medication adherence and perceived stress only significantly differed from zero for men such that a higher level of self-reported perceived stress was significantly related to a greater proportion of missed medication doses at baseline (t = 2.962, p =0.004). In contrast, perceived stress did not account for any variance in baseline medication adherence for women (t = 0.091, p =0.927).

Longitudinal Prediction to Medication Adherence Moderated by Gender

To test the hypothesis that the ability of PPSV to predict medication adherence over time differs depending on participant gender, three separate hierarchical multiple regression analyses were conducted for each independent variable. All analyses added an interaction term between gender and PPSV to the model and tested whether the prediction to medication adherence over time by each PPSV significantly differed between men and women. With the exception of perceived stress (γ_{12} = 0.00052, t (150) =

2.577, $p = 0.011$), gender did not moderate the prediction to medication adherence over time from baseline PPSV. After dummy coding females to 0, an additional regression analysis was performed and found that, for females, greater baseline pessimism significantly predicted a greater proportion of missed medication doses over time ($\gamma_{11} = 0.00093$, t (150) = 2.055, $p = 0.042$). Additionally, higher levels of reported baseline substance use ($\gamma_{11} = -0.00355$, t (150) = -2.053, $p = 0.042$), a higher number of reported negative life events ($\gamma_{11} = 0.00215$, t (150) = 2.577, $p = 0.011$), and greater perceived stress at baseline ($\gamma_{11} = 0.00074$, t (150) = 3.107, $p = 0.002$) significantly predicted a greater proportion of missed medication doses over time for females. To test the same hypotheses for males, males were dummy coded to 0 and the regression was repeated. Optimism ($\gamma_{11} = 0.00010$, t (150) = 0.817, $p = 0.415$), substance use ($\gamma_{11} = -0.00043$, t (150) = -0.839, $p = 0.403$), and negative life events (γ_{11} 0.00114, t (150) = 1.560, p = 0.121) did not significantly predict medication adherence over time for males. Perceived stress, however, was the only PPSV to significantly predict change in medication adherence over time for males ($\gamma_{11} = 0.00022$, t (150) = 2.743, $p = 0.007$) such that greater levels of perceived stress at baseline significantly predicted higher proportion of missed medication doses over time.

Summary: Psychosocial Variables, Adherence, and Gender

Gender did not moderate the relationship between positive psychosocial variables and medication adherence cross-sectionally or over time (hypothesis 3b). There was mixed support for hypothesis 4b. There was no significant difference between men and women with regard to the correlation between or prediction from avoidance coping to

medication adherence. Cross-sectionally, the correlation between higher perceived stress and worse medication adherence was significant for men only. Over time, higher perceived stress significantly predicted worse medication adherence in both men and women but was a significantly stronger predictor for women. Alcohol use was not correlated with medication adherence for men or women; over time, however, alcohol use at baseline significantly predicted worse medication adherence for women only. Lastly, the above findings suggest that the correlation that between worse medication adherence and a greater number of negative life events was significantly stronger for men than women. Negative life events, however, were more strongly predictive of worse medication adherence over time for women than men.

Cross-sectional Relationship between Negative Life Events and Depression Mediated by PPSV

Negative life events was not a significant predictor of depressive symptoms over time, therefore longitudinal mediation analyses were not performed. Cross-sectionally, however, negative life events was significantly related to depressive symptoms ($\beta = 0.434$, $p < 0.001$), as were all of the positive and negative psychosocial variables with the exception of benefit finding (see section titled *Cross-sectional Relationship to Depression*). Additional regression analyses showed that negative life events were significantly correlated with each of the PPSV with the exception of medication adherence ($\beta = 0.121$, $p = 0.160$). Therefore, the first three requirements for a cross-sectional mediation were significant for all PPSV except for benefit finding and medication adherence. Step 4 of the mediation analyses revealed that, when controlling

for all PPSV, negative life events were still a significant correlate of depressive symptoms scores (see table XX, column "*p for NLE*"). Sobel tests were conducted for each PPSV showing partial mediations of the model by 5 PPSV including social support ($z = 2.62$, $p = 0.008$), optimism ($z = 2.78$, $p = 0.005$), avoidance coping ($z = 2.01$, $p = 0.044$), substance use ($z = 1.93$, $p = 0.053$), and perceived stress ($z = 4.02$, $p = 0.001$).

Summary: Mediation between Psychosocial Variables and Depression

Hypothesis 6 was partly supported as it was found that social support, optimism, avoidance coping, substance use, and perceived stress partially mediated the relationship between negative life events and depressive symptoms cross-sectionally but not over time as negative life events did not significantly predict depressive symptoms.

Prediction from Negative Life Events to Medication Adherence Mediated by PPSV

Negative life events were not significantly correlated with medication adherence cross-sectionally, therefore cross-sectional mediation analyses were not performed. Over time, however, negative life events significantly predicted worse medication adherence ($\gamma_{11} = 0.001733$, t (151) = 2.843, $p = 0.005$), as did optimism, avoidance coping, perceived stress, and depressive symptoms (see table 25). Additional hierarchical regression analyses revealed that, when controlling for depressive symptoms, negative life events were no longer a significant predictor of medication adherence ($p = 0.096$), while depressive symptoms remained significant ($\gamma_{11} = 0.000251$, t (151) = 2.4763, $p = 0.014$). This suggests that depressive symptoms mediates the relationship between negative life events and medication adherence over time. Avoidance coping ($\gamma_{11} =$ -

0.000733, t (151) = -2.110, p = 0.037) and perceived stress (γ_{11} = 0.000237, t (151) = 3.200, p = 0.002), were significant predictors of worse medication adherence when controlling for negative life events, but negative life events remained significant in the model which did not indicate mediation.

Summary: Mediation between Psychosocial Variables and Adherence

Hypothesis 7 was partly supported as it was found that depressive symptoms mediated the relationship between negative life events and medication adherence over time but not cross-sectionally as negative life events was not significantly correlated with medication adherence cross-sectionally.

Chapter 5: Discussion

Depression

Congruent with previous research(Moskowitz, et al., 2010; Olley, et al., 2004; Packenham & Rinaldis, 2001), positive and negative psychosocial variables were correlated respectively with less and more depressive symptoms at baseline with exception of benefit finding, which was not significantly correlated with or predictive of depressive symptoms. It is possible that this was due to the smaller sample size for that particular variable (103 versus 177). Additionally, higher levels of baseline depressive symptoms were significantly correlated with poorer medication adherence, a finding that is also consistent with previous literature (Starace, et al., 2002). Our data did not, however, support the hypotheses that positive and negative psychosocial variables would respectively predict less and more depressive symptoms over time. There are several possible explanations for this. First, although there was significant individual variation in the slope of depressive symptoms scores over time, there was no significant change in depressive symptoms over time. Second, our sample reported relatively low levels of depressive symptoms as the average depressive symptoms score for each time point hovered around 10, a score 4 points below the cut-off for a mild depression diagnosis.

Depression moderated by gender

The hypothesis that positive psychosocial variables would be more strongly related to less depressive symptoms in women than men was not supported by our data. In fact, only the cross-sectional relationship between adaptive coping and depressive

symptoms significantly differed between men and women. Specifically, adaptive coping was related to lower levels of depressive symptoms for men but was unrelated to depressive symptoms for women, a finding opposite to that hypothesized. The non-significant relationship between adaptive coping and depressive symptoms for women conflicts with previous findings by Simoni & Ng (2006) which showed that adaptive coping was related to lower depression in WLWH. Of note, the sample size of women in the present study was smaller than Simoni & Ng, (2006) and may have been insufficient to detect a significant relationship. Previous research has, however, found that adaptive coping is related to less depression in MLWH (Penedo, et al., 2001). To our knowledge, the finding that gender fully moderates the relationship between adaptive coping and depressive symptoms such that it is significantly related to lower levels of depressive symptoms in men is unique and marks a possible future direction for further research.

Additional positive psychosocial variables significantly related to less depressive symptoms for both men and women included optimism and social support. The finding that social support is equally correlated to fewer depressive symptoms for both men and women supports findings that social support is related to better psychosocial functioning for both genders (Packenham & Rinaldis, 2001). Optimism has also previously been related to better psychosocial functioning in PLWH thus our finding is congruent with previous literature (Ironson, Balbin, et al., 2005). Despite previous literature as well as the means in our study suggesting that religious/spiritual coping is more frequently employed by women (Olley, et al., 2004; McIntosh & Rosselli, 2012, Sherr, et al., 2011; Tarakeshwar, et al., 2005), our study found a significant relationship between the use of religious/spiritual coping and lower levels of depressive symptoms for men but a non-

significant relationship for women. This result also may have been impacted by the smaller sample size of women in the present study. Additionally, this finding could suggest that religious coping is more strongly associated with lower levels of depressive symptoms for men than women.

Another possible explanation for this finding is that the majority of men in the present sample self-identified as gay, a sexual orientation that is traditionally rejected by mainstream religious institutions. It is possible that these men, as a result of having previously faced rejection from organized religious institutions, had found a more individualized, deeper connection with their own personal understanding of religion or spirituality and as such found it to be a stronger source of comfort and strength when coping with adversity.

Our data supported the hypothesis that negative psychosocial variables would be correlated with more depressive symptoms in both men and women. Specifically, our study found that greater alcohol use was more strongly correlated with greater levels of depressive symptoms in men than women, though the correlation was significant for both genders. This is congruent with previous literature (Olley, et al., 2004; Sherr, et al., 2011). Interestingly, over time alcohol use predicted greater levels of depressive symptoms in women but did not for men, a finding that to our knowledge is unique in the literature and worthy of further investigation.

As hypothesized, avoidance coping was equally related to greater depressive symptoms in men and women cross-sectionally. In contrast to our hypothesis that the relationship would be stronger for women, perceived stress and negative life events were equally correlated with depressive symptoms for both genders.

Lastly, suboptimal medication adherence was only significantly correlated with greater depressive symptoms for men but was unrelated for women. Sub-optimal medication adherence also significantly predicted greater depressive symptoms over time in men but did not for women. Very few studies have examined the contribution of gender to the relationship between medication adherence and psychosocial wellbeing in PLWH; therefore this is a unique finding that should be further investigated in future research.

Depression and Negative Life Events mediated by Psychosocial Variables

As negative life events did not significantly predict depressive symptoms over time, no longitudinal mediation analyses were performed. Cross-sectionally, however, depressive symptoms were significantly related to negative life events. None of the psychosocial variables fully mediated the relationship between negative life events and depressive symptoms, though there was support for partial mediation with five psychosocial variables. Specifically, positive psychosocial variables including social support and optimism decreased the impact of negative life events on depressive symptoms. In contrast, negative psychosocial variables including avoidance coping, alcohol use, and perceived stress exacerbated the effect and was associated with greater depressive symptoms.

Medication Adherence

Our study contrasts with previous research correlating positive psychosocial variables such as adaptive coping with better medication adherence as we found no significant correlations (DiMatteo, 2004; Ironson & Kremer, 2010). Over time, however, higher levels of dispositional optimism significantly predicted better medication

adherence. Gender impacted this relationship such that optimism predicted better adherence in women but not men. Research on this relationship is mixed. Findings supporting this relationship have demonstrated that those with higher levels of optimism tend to engage in more health-promoting behaviors (Scheier & Carver, 1985) such as condom use (Taylor, et al., 1992), medication adherence (Ironson, Balbin, et al., 2005), and exercise (Scheier, et al., 1989) and those PLWH that are more optimistic have slower disease progression (Ironson, Balbin, et al., 2005). However, other literature has related optimistic beliefs about disease prognosis with poorer medication adherence and high risk sexual behavior (Holmes & Pace, 2002). Additionally, there is a paucity of research examining gender differences in psychosocial factors related to adherence in PLWH (Berg, et al., 2004). Therefore, further investigation into this predictive relationship is needed.

Our study supports the well-documented correlational and predictive relationship between depressive symptoms and medication adherence (Starace, 2002) as well as perceived stress and medication adherence (Gifford, et al., 2000). Pre-existing literature on perceived stress has also correlated it with decreased adherence self-efficacy or the belief that one is able to be adherent to medication regimens (Johnson, et al., 2007). Interestingly, the relationship between perceived stress and medication adherence differed by gender cross-sectionally such that the relationship was significant for men but not women. Over time, however, this relationship was reversed. Perceived stress significantly predicted poorer adherence for both genders but was a significantly stronger predictor of poor adherence in women.

While avoidance coping and negative life events were not significantly correlated with medication adherence, they were predictive of poorer medication adherence over time. This corresponds with previous research findings in women only (Vyavaharkar, M. et al., 2007) for avoidance coping and in both genders for negative life events (Leserman, Ironson, et al., 2008). There were no gender differences in the predictive relationship between avoidance coping and adherence. There were, however, gender differences for negative life events. Cross-sectionally, gender moderated the relationship between negative life events and adherence. Negative life events significantly correlated with poor adherence for men but not women. Much like perceived stress, this relationship was reversed over time. More negative life events at baseline significantly predicted poorer adherence in women but was not a significant predictor for men. Again, due to limited research examining gender differences in such relationships, the above findings suggest that further research is needed.

Surprisingly, there was no significant correlational or predictive relationship between medication adherence and alcohol use despite previous literature consistently documenting this relationship in similar populations (Azar, Springer, Meyer, & Altice, 2010; Golin, et al., 2002; Chesney, et al., 2000; Gordillo, et al., 1999). Although not cross-sectionally correlated, alcohol use at baseline did significantly predict poorer adherence over time in women but not men. This finding is consistent with existing literature and suggests that the impact of alcohol use on adherence differs by gender and is more deleterious for women (Berg, et al., 2004; Howard, et al., 2002; Murphy, et al., 2002).

Medication adherence and negative life events mediated by psychosocial variables

Criteria for cross-sectional mediation were not met as negative life events were not related to medication adherence. Over time, however, negative life events predicted poorer adherence, and depressive symptoms met criteria as a mediator of the negative life events-adherence predictive relationship. This is congruent with previous research as depression is predictive of poor adherence (Starace, 2002) and negative life events are predictive of poor adherence as well (Leserman, Ironson, et al., 2008). Negative life events and depression have also previously been related in PLWH (Leserman, J., 2008). Our finding suggests that the way in which negative life events impact adherence is through depressive symptoms such that those who experience such stressors consequently experience an increase in depressive symptoms which in turn leads to worse adherence.

Summary

To summarize, depressive symptoms were correlated with all positive and negative psychosocial variables (optimism, social support, religious coping, adaptive coping, avoidance coping, alcohol use, negative life events, and medication adherence) with the exception of benefit finding. Gender moderated the relationship between adaptive coping and depressive symptoms, indicating that men who employ adaptive coping skills have fewer depressive symptoms than women. Religious coping and poorer medication adherence also significantly correlated with fewer depressive symptoms for only men, though gender did not moderate these relationships. Optimism, social support, avoidance coping, alcohol use, and perceived stress partially mediated the relationship between negative life events and depressive symptoms. None of the psychosocial

variables predicted depressive symptoms over time for all study participants. Gender did, however, moderate the predictive relationship between poor adherence and depressive symptoms, indicating that poor adherence predicted worse depressive symptoms in men only. Alcohol use predicted greater depressive symptoms over time for women only though gender did not moderate this relationship.

Positive psychosocial variables were not correlated with medication adherence. Over time, however, optimism predicted better adherence. Perceived stress and depressive symptoms correlated with and predicted to poorer adherence. Additionally, although not cross-sectionally correlated for the entire study sample, avoidance coping and negative life events significantly predicted poorer adherence. Gender, however, moderated the cross-sectional relationship between negative life events and medication adherence indicating that men who experience negative life events have worse adherence while there is no correlation for women. Negative life events significantly predicted poor adherence in women but gender did not moderate this finding. Perceived stress also significantly correlated with poorer adherence in men only but was predictive of poor adherence for women only though gender did not moderate these relationships. Depressive symptoms significantly predicted poor adherence for both genders.

Overall, the results of this dissertation suggest that positive and negative psychosocial variables have greater predictive power with more instrumental activities such as medication adherence than for depression as measured by level of depressive symptoms but correlate more strongly with depression in PLWH. Additionally, the results of this dissertation suggest that different psychosocial variables correlate with and predict both depression and medication adherence differently depending on gender of

PLWH. The timing of the impact of several psychosocial variables on depression and medication adherence also differs by gender such that psychosocial variables may have a more immediate impact on depression and adherence in men (i.e. correlate cross-sectionally) while their impact in women seems to develop over time. Additionally, those psychosocial variables traditionally associated poor medication adherence seem to impact depression in men and is predictive of worse depression in men over time.

Clinical Implications of Findings

Several results of this study have significant clinical implications that could positively impact the care of and treatment for PLWH. First, positive and negative psychosocial variables were found to mediate the cross-sectional relationship between negative life events and depression. Specifically, optimism and social support were found to decrease the impact of negative life events on depression while avoidance coping, alcohol use, and perceived stress were found to exacerbate the effect of negative life events on depression. Additionally, optimism was shown to predict better medication adherence over time. As previously noted, depression is a primary predictor of poor medication adherence and has been related to high risk behavior in PLWH thereby increasing the risk of disease progression and transmission. Additionally, stressful life events are inevitable in PWLH (Kremer & Ironson, 2010). Therefore, these findings indicate that a stress management intervention provided to PWLH at any time following diagnosis may bolster stress management skills and buffer the impact of stressful life events on psychosocial wellbeing. Group-based cognitive behavioral stress management interventions have been shown to be effective in decreasing depression in PWLH and to

improve coping skills in previous literature (Carrico, et al., 2006;). Our findings suggest that perhaps such interventions should be offered to PLWH prior to stressful events occurring to bolster their repertoire of coping skills. Our findings further suggest that such an intervention should highlight the importance of self-care such as decreased alcohol use (especially in women) and provide cognitive restructuring skills for increased optimism. These targeted topics may help prevent increases in depression and decreases in medication adherence over time. Because social support also buffers the impact of stressful life events on depression, such an intervention may be most impactful in a group format.

Additionally, gender differences in psychosocial factors affecting depression and medication adherence may indicate that interventions for these difficulties perhaps should be gender specific. Additionally, the timing of interventions to achieve maximum effectiveness with minimum negative effects on depression and adherence may also differ by gender as psychosocial variables were more frequently correlated with adherence and depression for men but were more frequently predictive for women. Men may require more immediate, tertiary interventions targeting behavior change while women may require more preventative care to deter the development of any possible negative impact. Lastly, the finding that alcohol use predicts poorer adherence in women may indicate that a thorough assessment of alcohol use in women is warranted and that women should be strongly encouraged to reduce consumption or abstain all together.

Limitations and Future Directions

This study had several limitations. First, it is of note that the women in our sample were predominantly African American, self-identified as heterosexual, and of low socioeconomic status while the men in our sample were predominantly Caucasian, self-identified as gay, and were middle class. Therefore, the gender moderated effects found in this study may have been influenced by these demographic differences. Further research should re-examine these gender effects in a more demographically congruent sample of men and women. Additionally, the smaller sample size for women may have contributed to our study detecting a simple effect between medication adherence and depression for men but not women. Future research should also re-examine gender differences in a sample comprised more equally of men and women.

Another limitation was our study's reliance on self-report measures for both medication adherence and depression. Participants tended to report a high degree of compliance with medication regimens which may have been influenced by a widely recognized positive response bias for such self-report measures (Wagner, 2002). Participants also tended to report low levels of depression which may also have been influenced by a desire to appear more emotionally stable. Future research should utilize strategies for increasing the response accuracy and minimizing the impact of social response bias such as more objective measurements of adherence (MEMS caps, tracking prescription refills) or employing several self-report measures for the same construct to ensure consistency.

Lastly, the number of gender moderated effects found in our study suggests that future research should take gender into consideration when examining psychosocial

wellbeing and adherence in PLWH. Intervention studies aimed towards increasing adherence or decreasing psychosocial distress should consider how gender may influence the timing, impact, and effectiveness of intervention strategies. Additionally, future research should continue to examine contributions of psychosocial factors on wellbeing and health behaviors in PLWH.

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Appendix: Tables

Table 1: Descriptive Demographics of Participant Sample

Demographics	*Total Sample*		*Males*		*Females*	
	N	*%*	*N*	*%*	*N*	*%*
Gender						
Male	124	70.5				
Female	52	29.5				
Ethnicity						
Caucasian	54	30.5	35	28.2	19	35.8
African American	64	36.2	48	38.7	16	30.2
Hispanic	50	28.2	35	28.2	15	28.3
Other*	8	4.5	6	4.8	2	3.8
Education						
Less than High School	32	18.3	15	12.1	17	33.3
High School Graduate	24	13.6	11	8.9	13	24.5
Some College/Trade School	71	40.1	52	43.0	19	35.8
College Graduate	34	19.2	34	27.4	0	0
Graduate Degree	14	7.9	12	9.7	2	3.8

Table 2. BDI-II Scores at each time point

Time Point	*N*	*Mean*	*S*
Baseline	176	11.35	8.89
Time 1 (6 months)	154	9.54	8.52
Time 2 (1 year)	139	9.67	9.37
Time 3 (1 year 6 months)	125	8.76	8.27
Time 4 (2 years)	120	8.76	8.96

Table 3. ACTG Scores at each time point

Time Point	*N*	*Mean*	*S*
Baseline	125	0.098	0.228
Time 1 (6 months)	116	0.096	0.220
Time 2 (1 year)	118	0.086	0.201
Time 3 (1 year 6 months)	104	0.087	0.226
Time 4 (2 years)	103	0.125	0.286

Table 4. Descriptive Statistics for Positive and Negative Psychosocial Variables at baseline

PPSV	*N*	*Mean*	*S*
Social Support	177	22.38	6.11
Low Optimism	176	16.85	5.00
Religious Coping	177	5.35	2.29
Benefit Finding	103	59.65	17.26
Maladaptive Coping	177	14.27	2.42
Substance Use	177	7.09	1.52
Perceived Stress	177	17.67	7.04
Negative Life Events	177	1.08	1.64
Adaptive Coping	177	23.29	5.71

Table 5. Descriptive Statistics for Positive and Negative Psychosocial Variables at baseline for males

PPSV	*N*	*Mean*	*S*
Social Support	124	21.90	6.37
Low Optimism	123	16.67	5.12
Religious Coping	124	5.08	2.34
Benefit Finding	67	59.10	18.04
Maladaptive Coping	124	14.44	2.37
Substance Use	124	7.00	1.61
Perceived Stress	124	17.56	7.25
Negative Life Events	124	0.911	1.31
Adaptive Coping	124	23.68	5.46

Table 6. Descriptive Statistics for Positive and Negative Psychosocial Variables at baseline for females

PPSV	*N*	*Mean*	*S*
Social Support	53	23.53	5.34
Low Optimism	53	17.26	4.74
Religious Coping	53	5.96	2.08
Benefit Finding	36	60.67	15.88
Maladaptive Coping	53	13.85	2.50
Substance Use	53	7.30	1.28
Perceived Stress	53	17.92	6.60
Negative Life Events	53	1.49	2.19
Adaptive Coping	53	22.38	6.21

Table 7. Independent Samples t-test on Gender Differences in PPSV

PPSV	*Levene's Test for equality of variance*		*Independent Samples T-Test*		
	F	*p*	*t*	*df*	*p*
Adherence	0.824	0.366	0.491	123	0.624
Social Support	1.027	0.312	-1.635	175	0.104
Low Optimism	0.936	0.335	-0.726	174	0.469
Religious Coping*	3.818	0.052	-2.484	109.48	0.015**
Benefit Finding	1.232	0.270	-0.436	101	0.664
Adaptive Coping	1.906	0.169	1.392	175	0.166
Maladaptive Coping	0.689	0.408	1.505	175	0.134
Substance Use	2.374	0.125	-1.212	175	0.227
Perceived Stress	3.053	0.082	-0.313	175	0.755
Negative Life Events*	13.798	<0.001	-1.793	68.53	0.077
Depressive Symptoms	0.133	0.716	0.751	175	0.454

*equal variances not assumed
**significant at the 0.05 level

Table 8. Cross-Sectional Relationship between Baseline Depressive Symptoms and Adaptive Coping

Variable	*B*	*SE B*	*β*	*t*	*p*
Adaptive Coping	-0.463	0.112	-0.297	-4.122	0.000*
Age	0.058	0.075	0.058	0.769	0.443
Gender	3.369	1.527	0.174	2.207	0.029
Ethnicity	0.497	0.719	0.050	0.692	0.490
Education	-1.286	0.426	-0.241	-3.017	0.003

Table 9. Cross-Sectional Relationship between Baseline Depressive Symptoms and Positive and Negative Psychosocial Variables
(n = 176)

Variable	*B*	*SE B*	*β*	*t*	*p*
Social Support	-0.606	0.098	-0.422	-6.176	0.000
Low Optimism	1.119	0.104	0.640	10.738	0.000
Religious Coping	-0.741	0.287	-0.194	-2.582	0.011
Benefit Finding	0.072	0.052	0.139	1.382	0.170
Maladaptive Coping	-1.214	0.265	-0.334	-4.584	0.000
Substance Use	-2.000	0.414	-0.347	-4.825	0.000
Perceived Stress	0.706	0.079	0.558	8.950	0.000
Medication Adherence	6.767	3.411	0.182	1.984	0.050
Negative Life Events	2.319	0.3680	0.434	6.295	0.000

Table 10. Basic Model including Coefficients and Significance Tests for Level 1 and Level 2 Covariates in Prediction of Slope of Depressive Symptoms over 2 Years controlling for baseline depressive symptoms (n=174)

	Coefficient	Standard Error	*t* Ratio	*df*	*p*
Fixed effects					
Depression intercept, β_0					
Intercept, γ_{00}	9.6705	0.9435	10.250	171	<0.001
Depresion slope (per month), β_1					
Average slope, γ_{10}	0.42979	0.2062	2.085	165	0.039
Adaptive coping, γ_{11}	-0.00147	0.0049	-0.302	165	0.763
Age, γ_{12}	-0.00762	0.0033	-2.349	165	0.020
Gender, γ_{13}	-0.17678	0.0680	-2.599	165	0.010
Ethnicity, γ_{14}	-0.04348	0.0325	-1.337	165	0.183
Education, γ_{15}	-0.03861	0.0194	-1.987	165	0.049
Baseline Depressionγ_{16}	0.00764	0.0033	2.293	165	0.023
Antiretroviral 1 increment, β_2					
Average increment, γ_{20}	0.59204	1.5727	0.376	323	0.707
Antiretroviral 2 increment, β_3					
Average increment, γ_{30}	1.00030	1.1935	0.838	323	0.403
Antiretroviral 1 increment over time, β_4					
Average increment over time, γ_{40}	-0.00746	1.1050	-0.071	323	0.943
Antiretroviral 2 increment over time, β_5					
Average increment over time, γ_{50}	-0.03696	0.0760	-0.486	323	0.627
Random effects	SD	Variance	df	χ^2	*p* Value
Intercept, U_0	6.646	44.168	169	405.330	0.000
Slope, U_1	0.032	0.1032	164	291.414	0.000
Error, *R*	6.505	42.309			

Table 11. Prediction from Positive and Negative Psychosocial Variables to Slope of Depression controlling for baseline depression

Predictor	Main Analyses (*n=174*)		
	γ11 γ coefficient	*t* Ratio	*p*
Social Support	-0.003397	-0.611	0.542
Low Optimism	-0.002440	-0.362	0.718
Religious Coping	0.009722	0.870	0.386
Benefit Finding (n=102)	-0.001333	-0.661	0.510
Maladaptive Coping	0.014493	1.125	0.262
Substance Use	0.021469	1.132	0.259
Perceived Stress	-0.004520	-0.894	0.372
Medication Adherence (n=123)	0.209009	1.426	0.157
Negative Life Events	-0.006491	-0.357	0.722

*Covariates included age, gender, ethnicity, and education for each analysis

Table 12. Cross-Sectional Relationship between Baseline Depressive Symptoms and Adaptive Coping Moderated by Gender

Variable	*B*	*SE B*	*t*	*p*
Adaptive Coping	-0.057	0.195	-0.292	0.770
Age	0.034	0.075	0.452	0.652
Gender	17.615	5.829	3.022	0.003
Gender*AdaptC	-0.607	0.240	-2.530	0.012
Ethnicity	0.571	0.708	0.807	0.421
Education	-1.435	0.424	-3.388	0.001

R2 = 0.172: F= 5.781; p<0.001
ΔR2 = 0.032; F= 6.399; p=0.012*
Males Dummy Coded = 1

Variable	*B*	*SE B*	*t*	*p*
Adaptive Coping	-0.664	0.136	-4.877	<0.001
Age	0.034	0.075	0.452	0.652
Gender	-17.615	5.829	-3.022	0.003
Gender*AdaptC	0.607	0.240	2.530	0.012
Ethnicity	0.571	0.708	0.807	0.421
Education	-1.435	0.424	-3.388	0.001

R2 = 0.085: F= 1.805; p=0.104
ΔR2 = 0.016; F= 2.020; p=0.158
Females Dummy Coded = 1

Table 13. Cross-Sectional Relationship between Baseline Depression and Positive and Negative Psychosocial Variables Moderated by Gender
(n = 174)

Variable	*B*	*SE B*	*t*	*p*	*R2*	*ΔR2*	*F*	*p (mod)*
Social Support - F	-0.819	0.210	-3.894	**<.001**	0.235		8.527	<.001
Social Support – M	-0.547	0.111	-4.930	**<.001**				
Social support*Gen	0.272	0.238	1.145	0.254		0.006	1.311	0.254
Low Optimism - F	1.079	0.217	4.966	**<.001**	0.430		20.888	<.001
Low Optimism – M	1.131	0.119	9.502	**<.001**				
Low Optimism*Gen	0.052	0.247	0.210	0.834		0.000	0.044	0.834
Religious Coping - F	-0.539	0.593	-0.909	0.365	0.090		2.762	0.014
Religious Coping- M	-0.804	0.331	-2.431	**0.016**				
Religious Coping*Gen	-0.265	0.682	-0.389	0.357		0.001	0.151	0.698
Benefit Finding -F	0.129	0.097	1.324	0.189	0.080		1.370	0.235
Benefit Finding-M	0.048	0.063	0.771	0.442				
Benefit Finding*Gen	-0.080	0.116	-0.688	0.493		0.005	0.474	0.493
Maladapt Coping -F	-1.584	0.471	-3.364	**0.001**	0.163		5.425	<.001
Maladapt Coping –M	-1.049	0.317	-3.309	**0.001**				
Maladaptive Coping*Gender	0.535	0.563	0.951	0.343		0.005	0.903	0.343
Substance Use -F	-2.456	0.908	-2.705	**0.008**	0.170		5.706	<.001
Substance Use –M	-1.882	0.465	-4.051	**<.001**				
Substance Use*Gender	0.574	1.016	0.566	0.572		0.002	0.320	0.572
Perceived Stress -F	0.840	0.166	5.066	**<.001**	0.362		15.804	<.001
Perceived Stress- M	0.668	0.089	7.466	**<.001**				
Perceived Stress*Gender	-0.173	0.188	-0.918	0.360		0.003	0.843	0.360
Med Adherence -F	2.854	8.653	0.330	0.742	0.079		1.667	0.135
Med Adherence –M	7.508	3.739	2.008	**0.047**				
Med Adherence*Gender	4.654	9.454	0.492	0.623		0.002	0.242	0.623
Neg Life Events -F	2.371	0.502	4.726	**<.001**	0.234		8.507	<.001
Neg Life Events – M	2.256	0.550	4.102	**<.001**				
Negative Life Events*Gender	-0.116	0.747	-0.155	0.877		0.000	0.024	0.877

All Variables with –F = Males dummy coded 1
All Variables with –M = Females dummy coded 1

Table 14. Basic Model including Coefficients and Significance Tests for Level 1 and Level 2 Covariates in Prediction of Slope of Depression over 2 Years Moderated By Gender controlling for baseline depression

	Coefficient	Standard Error	*t* Ratio	*df*	*p*
Fixed effects					
Depression intercept, β_0					
Intercept, γ_{00}	9.676	0.942	10.273	171	<0.001
Depresion slope (per month), β_1					
Average slope, γ_{10}	0.1423	0.1997	0.713	164	0.477
Adaptive coping (female), γ_{11}	-0.0047	0.0076	-0.611	164	0.542
Adaptive coping (male), γ_{11}	0.0006	0.0063	0.103	164	0.918
Adaptive coping*Gender γ_{12}	0.0053	0.0098	0.543	164	0.588
Age, γ_{13}	-0.0074	0.0033	-2.277	164	0.024
Gender, γ_{14}	0.0505	0.2570	0.197	164	0.844
Ethnicity, γ_{15}	-0.0453	0.0320	-1.416	164	0.159
Education, γ_{16}	-0.0370	0.0198	-1.871	164	0.063
Baseline Depression, γ_{17}					
Antiretroviral 1 increment, β_2					
Average increment, γ_{20}	0.0608	1.5721	0.387	323	0.699
Antiretroviral 2 increment, β_3					
Average increment, γ_{30}	0.9921	1.1946	0.830	323	0.407
Antiretroviral 1 increment over time, β_4					
Average increment over time, γ_{40}	-0.0065	0.1047	-0.062	323	0.951
Antiretroviral 2 increment over time, β_5					
Average increment over time, γ_{50}	-0.0360	0.0762	-0.473	323	0.637
Random effects	SD	Variance	df	χ^2	*p* Value
Intercept, U_0	6.6488	44.2061	169	405.34	<0.001
Slope, U_1	0.3230	0.10436	163	291.71	<0.001
Error, *R*	6.5041	42.3028			

*Adaptive Coping (female) = females dummy coded 0

*Adaptive Coping (males) = males dummy coded 0

Table 15. Prediction from Positive and Negative Psychosocial Variables to Slope of Depressive Symptoms Moderated by Gender controlling for baseline depressive symptoms

Predictor	Main Analyses (*n=174*)			
	γ16 γ coefficient	γ17 γ coefficient	*t* Ratio	*p*
Social Support – F	0.0097		1.168	0.245
Social Support - M	-0.0078		-1.215	0.226
Social Support*Gender		-0.0174	-1.796	0.074
Low Optimism - F	-0.0123		-0.935	0.351
Low Optimism – M	0.0003		0.045	0.964
Low Optimism*Gen		0.0126	1.011	0.313
Religious Coping –F	0.0263		1.388	0.167
Religious Coping -M	0.0033		0.235	0.814
Religious Coping*Gender		-0.0230	-0.940	0.349
Benefit Finding – F	-0.0027		-0.792	0.431
Benefit Finding - M	-0.0006		-0.265	0.792
Benefit Finding*Gender		0.0021	0.495	0.622
Maladapt Coping-F	0.0213		1.137	0.257
Maladapt Coping -M	0.0113		0.727	0.469
Maladaptive Coping*Gender		-0.0098	-0.434	0.665
Substance Use – F	0.0581		2.208	**0.029**
Substance Use - M	0.0101		0.462	0.645
Substance Use*Gender		-0.0480	-1.505	0.134
Perceived Stress – F	-0.0157		-1.787	0.076
Perceived Stress - M	-0.0015		-0.279	0.781
Perceived Stress*Gender		0.0014	1.597	0.112
Med Adherence - F	-0.2640		-1.694	0.093
Med Adherence - M	0.3502		2.219	**0.029***
Medication Adherence*Gen		0.6142	2.787	**0.006***
Neg Life Events - F	-0.0288		-1.566	0.119
Neg Life Events - M	0.0253		0.854	0.394
Negative Life Events*Gender		0.0542	1.744	0.083

*Covariates included age, gender, ethnicity, and education for each analysis
All variables multiplied by gender covariate for moderation analysis
Females dummy coded to 0 for interaction terms
*significant at the 0.05 level
*n=123 for medication adherence
*n = 102 for benefit finding

Table 16. Cross-Sectional Relationship between Baseline Medication Adherence and Adaptive Coping

Variable	*B*	*SE B*	*β*	*t*	*p*
Adaptive Coping	-0.002	0.004	-0.045	-0.500	0.618
Age	0.001	0.002	0.029	0.311	0.757
Gender	0.084	0.049	0.164	1.694	0.093
Ethnicity	0.000	0.022	-0.002	-0.017	0.987
Education	-0.036	0.013	-0.271	-2.800	0.006

Table 17. Cross-Sectional Relationship between Baseline Medication Adherence and Positive and Negative Psychosocial Variables
(n = 125)

Variable	*B*	*SE B*	*β*	*t*	*p*
Social Support	0.001	0.003	0.035	0.378	0.706
Low Optimism	0.005	0.004	0.117	1.296	0.197
Religious Coping	0.009	0.009	0.089	0.974	0.332
Benefit Finding	0.001	0.001	0.150	1.254	0.214
Maladaptive Coping	-0.008	0.009	-0.079	-0.878	0.382
Substance Use	-0.003	0.014	-0.020	-0.215	0.830
Perceived Stress	0.008	0.003	0.236	2.695	0.008*
Depressive Symptoms	0.005	0.002	0.178	1.984	0.050*
Negative Life Events	0.023	0.014	0.150	1.680	0.096

Table 18. Basic Model including Coefficients and Significance Tests for Level 1 and Level 2 Covariates in Prediction of Slope of Proportion of Missed Medication Doses over 2 Years

	Coefficient	Standard Error	*t* Ratio	*df*	*p*
Fixed effects					
MedAd intercept, β_0					
Intercept, γ_{00}	1.100	0.174	6.329	156	.000
MedAd slope (per month), β_1					
Average slope, γ_{10}	-0.0215	0.0171	-1.257	151	0.211
Adaptive coping, γ_{11}	-0.0002	0.0001	-1.621	151	0.107
Age, γ_{12}	-0.0001	0.0001	-1.359	151	0.176
Gender, γ_{13}	0.0001	0.0014	0.066	151	0.948
Ethnicity, γ_{14}	-0.0007	0.0007	0.998	151	0.320
Education, γ_{15}	-0.0009	0.0005	-1.943	151	0.054
Antiretroviral 1 increment, β_2					
Average increment, γ_{20}	-1.006	0.176	-5.700	234	0.000
Antiretroviral 2 increment, β_3					
Average increment, γ_{30}	- 1.021	0.160	-5.757	234	0.000
Antiretroviral 1 increment over time, β_4					
Average increment over time, γ_{40}	0.031	0.017	1.828	234	0.069
Antiretroviral 2 increment over time, β_5					
Average increment over time, γ_{50}	0.029	0.017	1.747	234	0.082
Random effects	SD	Variance	df	χ^2	*p* Value
Intercept, U_0	0.144	0.021	142	247.24	0.000
Slope, U_1	0.006	0.00003	137	160.81	0.030
Error, *R*	0.187	0.035			

Table 19. Prediction from Positive and Negative Psychosocial Variables to Slope of Proportion of Missed Medication Doses

Predictor	Main Analyses (n = 174)		
	γ11 γ coefficient	*t* Ratio	*p*
Social Support	-0.000223	-1.503	0.135
Low Optimism	0.000311	2.015	0.046*
Religious Coping	-0.000476	-1.347	0.180
Benefit Finding***	0.000049	0.888	0.377
Maladaptive Coping	-0.000883	-2.439	0.016*
Substance Use	-0.001025	-1.673	0.096
Perceived Stress	0.000344	3.794	<0.001*
Depressive Symptoms	0.000344	3.560	<0.001*
Negative Life Events	0.001733	2.843	0.005*

Covariates included age, gender, ethnicity, and education for each analysis
*significant at the 0.05 level
***robust standard errors could not be calculated for this analysis due to maximum iterations reached before model convergence

Table 20. Cross-Sectional Relationship between Baseline Medication Adherence and Adaptive Coping Moderated by Gender

Variable	*B*	*SE B*	*t*	*p*
Adaptive Coping	0.005	0.006	0.849	0.397
Age	0.000	0.002	0.122	0.903
Gender	0.340	0.187	1.818	0.072
Gender*AdaptC	-0.011	0.008	-1.421	0.158
Ethnicity	0.002	0.022	0.097	0.923
Education	-0.039	0.013	-3.016	0.003

R2 = 0.085: F= 1.805; p=0.104
ΔR2 = 0.016; F= 2.020; p=0.158
Males Dummy Coded = 1

Variable	*B*	*SE B*	*t*	*p*
Adaptive Coping	-0.006	0.005	-1.271	0.206
Age	0.000	0.002	0.122	0.903
Gender	-0.340	0.187	-1.818	0.072
Gender*AdaptC	0.011	0.008	1.421	0.158
Ethnicity	0.002	0.022	0.097	0.923
Education	-0.039	0.013	-3.016	0.003

R2 = 0.085: F= 1.805; p=0.104
ΔR2 = 0.016; F= 2.020; p=0.158
Females Dummy Coded = 1

Table 21. Cross-Sectional Relationship between Baseline Medication Adherence and Positive and Negative Psychosocial Variables Moderated by Gender
(n = 125)

Variable	*B*	*SE B*	*t*	*p*	*R2*	*ΔR2*	*F*	*p (model)*
Social Support - F	0.008	0.008	1.014	0.313	0.076		1.584	0.158
Social Support – M	0.000	0.004	-0.071	0.943				
Social support*Gen	-0.008	0.009	-0.944	0.347		0.007	0.891	0.347
Low Optimism - F	-0.001	0.010	-0.072	0.943	0.077		1.602	0.153
Low Optimism – M	0.007	0.005	1.460	0.147				
Low Optimism*Gen	0.008	0.011	0.679	0.499		0.004	0.461	0.499
Religious Coping - F	0.017	0.019	0.924	0.357	0.077		1.618	0.148
Religious Coping- M	0.006	0.010	0.594	0.554				
Religious Coping*Gen	-0.011	0.022	-0.527	0.599		0.002	0.278	0.599
Benefit Finding -F	0.000	0.002	0.051	0.959	0.107		1.316	0.262
Benefit Finding-M	0.002	0.001	1.439	0.155				
Benefit Finding*Gen	0.002	0.002	0.718	0.475		0.007	0.516	0.475
Maladapt Coping -F	-0.015	0.017	-0.856	0.394	0.075		1.577	0.160
Maladapt Coping –M	-0.005	0.010	-0.506	0.614				
Maladaptive Coping*Gender	0.009	0.020	0.477	0.634		0.002	0.228	0.634
Substance Use -F	-0.018	0.037	-0.475	0.636	0.069		1.440	0.205
Substance Use –M	-0.001	0.015	-0.056	0.956				
Substance Use*Gender	0.017	0.040	0.425	0.671		0.001	0.181	0.671
Perceived Stress -F	0.001	0.007	0.091	0.927	0.133		2.968	**0.010***
Perceived Stress- M	0.009	0.003	2.962	**0.004***				
Perceived Stress*Gender	0.009	0.007	1.219	0.225		0.011	1.486	0.225
Dep. Symptoms -F	0.003	0.006	0.447	0.634	0.099		2.113	**0.057***
Dep. Symptoms –M	0.005	0.003	1.923	0.057				
Dep. Symptoms*Gen	0.002	0.007	0.297	0.767		0.001	0.088	0.767
Neg Life Events -F	-0.014	0.023	-0.610	0.543	0.121		2.655	**0.019***
Neg Life Events – M	0.045	0.017	2.591	**0.011***				
Negative Life Events*Gender	0.059	0.029	2.031	**0.044***		0.031	4.127	**0.044***

All Variables with –F = Males dummy coded 1
All Variables with –M = Females dummy coded 1

Table 22. Basic Model including Coefficients and Significance Tests for Level 1 and Level 2 Covariates in Prediction of Slope of Proportion of Missed Medication Doses over 2 Years Moderated by Gender

	Coefficient	Standard Error	*t* Ratio	*df*	*p*
Fixed effects					
MedAd intercept, β_0					
Intercept, γ_{00}	1.0946	0.1719	6.368	156	<0.001
MedAd slope (per month), β_1					
Average slope, γ_{10}	-0.01823	0.01782	-1.023	150	0.308
Adaptive coping females, γ_{11}	-0.000359	0.000251	-1.430	150	0.155
Adaptive coping males, γ_{11}	-0.00016	0.000178	-0.893	150	0.373
Adaptive Coping *Gender,γ_{12}	0.0002	0.0003	-0.648	150	0.518
Age, γ_{13}	-0.0001	0.0001	-1.149	150	0.252
Gender, γ_{14}	-0.0047	0.0079	-0.592	150	0.555
Ethnicity, γ_{15}	0.0007	0.0007	0.937	150	0.350
Education, γ_{16}	-0.0009	0.0005	-1.926	150	0.056
Antiretroviral 1 increment, β_2					
Average increment, γ_{20}	-1.0003	0.1748	-5.722	234	<0.001
Antiretroviral 2 increment, β_3					
Average increment, γ_{30}	-1.008	0.1739	-5.795	234	<0.001
Antiretroviral 1 increment over time, β_4					
Average increment over time, γ_{40}	0.0300	0.0166	1.814	234	0.071
Antiretroviral 2 increment over time, β_5					
Average increment over time, γ_{50}	0.0287	0.016	1.737	234	0.084
Random effects					
Intercept, U_0	0.1436	0.0206	142	246.55	<0.001
Slope, U_1	0.0056	0.0001	136	159.13	0.085
Error, R	0.1873	0.0351			

Males dummy coded to 1

Table 23. Prediction from Positive and Negative Psychosocial Variables to Slope of Medication Adherence Moderated by Gender

Predictor	Main Analyses (n = 174)			
	γ11 γ coefficient	γ12 γ coefficient	*t* Ratio	*p*
Social Support – F	-0.00041		-1.335	0.184
Social Support – M	-0.00016		-0.957	0.340
Social Support*Gen		0.0003	0.739	0.461
Low Optimism – F	0.00093		2.055	**0.042***
Low Optimism – M	0.00010		0.817	0.415
Low Optimism*Gen		0.00083	1.744	0.083
Religious Coping-F	-0.00123		-1.468	0.144
Religious Coping-M	-0.00017		-0.529	0.598
Religious Coping*Gender		-0.0011	-1.201	0.232
Benefit Find – F	0.00002		0.167	0.868
Benefit Find - M	0.00007		0.971	0.334
Benefit Finding*Gender		-0.0001	-0.440	0.661
Maladaptive – F	-0.00098		-1.701	0.091
Maladaptive – M	-0.00083		-1.775	0.078
Maladaptive Coping*Gender		-0.00015	-0.195	0.845
Alcohol Use – F	-0.00355		-2.053	**0.042***
Alcohol Use – M	-0.00043		-0.839	0.403
Alcohol Use*Gender		-0.0031	-1.727	0.086
Perceived Stress – F	0.00074		3.107	**0.002***
Perceived Stress - M	0.00022		2.743	**0.007***
Perceived Stress*Gender		0.00052	2.058	**0.041***
Dep. Symptoms – F	0.00057		3.184	**0.002***
Dep. Symptoms – M	0.00025		2.237	**0.027***
Dep Symptoms*Gen		0.00033	1.521	0.130
Neg Life Events - F	0.00215		2.577	**0.011***
Neg Life Events – M	0.00114		1.560	0.121
Negative Life Events*Gender		0.0010	0.911	0.364

*Covariates included age, gender, ethnicity, and education for each analysis
All variables multiplied by gender covariate for moderation analysis
Males dummy coded to 0 for interaction term
*significant at the 0.05 level

Table 24: Cross-Sectional Relationship between Baseline Depressive Symptoms and Negative Life Events Mediated by Significant Psychosocial Variables

Variable	*B*	*SE B*	*β*	*t*	*p*	*p for NLE*
Social Support	-0.490	0.093	-0.342	5.247	0.000	0.000
Low Optimism	0.998	0.098	0.571	10.157	0.000	0.000
Religious Coping	-0.621	0.260	-0.163	-2.386	0.018	0.000
Adaptive Coping	-0.424	0.101	-0.272	-4.177	0.000	0.000
Maladaptive Coping	-0.954	0.247	-0.262	-3.854	0.000	0.000
Substance Use	-1.622	0.385	-0.281	-4.214	0.000	0.000
Perceived Stress	0.588	0.080	0.464	7.316	0.000	0.000
Medication Adherence	4.505	3.186	0.121	1.414	0.160	0.000

*Covariates included age, gender, ethnicity, and education for each analysis

Table 25. PPSV as Mediator between Negative Life Events and the Slope of Medication Adherence

Predictor	Main Analyses (*n=123*)			
	γ11 γ coefficient	*t* Ratio	*p*	*p for NLE*
Low Optimism	0.000209	1.580	0.116	0.014
Maladaptive Coping	-0.000733	-2.110	0.037	0.008
Perceived Stress	0.000237	3.200	0.002	0.026
Depressive Symptoms	0.000251	2.476	**0.014**	**0.096**

*Covariates included age, gender, ethnicity, and education for each analysis