Variables related to viral load and CD4 variance in men with HIV

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ABSTRACT

In 2018, 37,968 individuals were diagnosed with HIV in the United States (CDC, 2018). Self-identified men made up 81% of all newly diagnosed cases, particularly men who have sex with men (CDC, 2020). Achieving viral load suppression allows men living with HIV to obtain optimal health, maintain quality of life, and prevent the virus's spread (Sax, 2012). Past research in HIV treatment has mainly focused on individual health behaviors, such as medication adherence, to account for the variances in these variables; however, the Social Determinants of Health (SDOH) and chronic conditions have gradually become a subject of HIV treatment research. SDOH's are defined by "the conditions in which people are born, grow, work, live, and age" (Bravemen et al., 2011, p.2). Chronic conditions, including; physical, mental health, and chronic pain, are defined as a chronic illness that lasts one year or more, requiring ongoing medical attention and affecting daily living (CDC, 2021). The purpose of this study was to test whether SDOH and chronic conditions, individually and collectively, influence viral load and CD4 count variance in men living with HIV. The sample consisted of 130 men living with HIV receiving services at a non-profit for HIV + individuals who were assessed for SDOH's and chronic illnesses. Results of Independent T-tests suggested that men who had insurance, income, and chronic pain had a higher mean viral load compared to men with an absence of these variables. In contrast, socially active men had a lower mean viral load than men who were not socially active. The multiple regression model using both groups explained more of the sample's viral load variance compared to the variables separately. The implication of the study's findings and future directions will be discussed.

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CHAPTER ONE: INTRODUCTION

Human Immunodeficiency Virus (HIV) continues to be a significant problem across the United States (CDC, 2018). The incurable virus attacks the T-cells or white blood cells of the body's immune system. Destroying T-cells exposes individuals to a higher risk of opportunistic infections, cancers, and potential death by advanced stage Acquired Immune Deficiency Syndrome (AIDS) (AVERT, 2019). In 2018, 37,968 individuals were diagnosed with HIV in the United States (CDC, 2018). Self- identified men made up 81% of all newly diagnosed cases, particularly men who have sex with men (MSM) (CDC, 2020). The main form of treatment for HIV is antiretroviral therapy (ART). ART supports the body's fight against HIV by supporting an individual's CD4 count (a type of T-cells) and decreasing viral load in the blood (AVERT, 2020). ART's ultimate goal is to reduce the viral load to reach viral suppression (viral level in a patient's blood is <20). Viral suppression allows people living with HIV (PLWH) to obtain optimal health, maintain quality of life, and prevent the virus's spread (Sax, 2012). Despite the importance of viral suppression, current statistics suggest that only 56 out of every 100 men with HIV were virally suppressed (CDC, 2018). Past research in HIV treatment has mainly focused on individual health behaviors, such as medication adherence, to account for the variance in CD4 and viral load in this population; however, individual actions have not accounted for all the variance in these variables. Social determinants of health (SDOH) have gradually become a subject of HIV treatment research. Once regarded as a minor influence on disease, SDOH has increasingly been used to understand chronic disease progression, including HIV health outcomes like CD4 count and viral load (Cockerham et al., 2017). Along with SDOH, literature has become more interested in the confounding effects of other types of chronic illnesses, including physical conditions, chronic pain, and mental health diagnoses that may affect these

health outcomes. Although these variables are gaining more recognition, little research has compared the effects of these variables on the variance in CD4 count and viral load in men living with HIV (MLWH). This study aims to understand how the variables of the SDH and chronic illness affect the viral load and CD4 variance in MLWH.

CHAPTER TWO: LITERATURE REVIEW

Social Determinants of Health

The Social Determinants of Health (SDOH) are defined by "the nonmedical factors influencing health, including health-related knowledge, attitudes, beliefs, and behaviors, or put simply; the conditions in which people are born, grow, work, live, and age" (Braveman et al., 2011, pg.2; Friedman, 2018). The interest in these social factors began in the 1980s as a response to the growing criticism in the United States that the longstanding research linking medical care and health outcomes could not explain the variance in health disparities worldwide and social position (Penman- Aguliar et al., 2016). As such, increased attention to how someone's social conditions impact health began to take root (Taylor et al., 2016). This attention to social conditions connected to the growing theoretical literature explaining the relationship between SDOH and disease (Cokerham et al., 2017). Theories related to SDOH can vary greatly depending on the research discipline; however, this review will focus on the 4 psychosocial theories commonly addressed in the SDOH literature to explain the etiology of disease.

The life-course theory suggests that individuals go through stages of age and social roles within particular social structures over their lives (Arcaya et al., 2015 Cockerham et al., 2017; Mortimer, 2003). The theory postulates that social factors, such as geography or poverty, affect a particular disease's origin and process (Arcaya et al., 2015). For example, the additive effect of living in poverty as a child has a long-term impact on that child's health as an adult (Cokerham et al., 2017). Another theoretical approach is called the fundamental course theory (Cokerham et al., 2017). Link and Phelan (2010) developed the theory to explain how a social variable can explain disease onset. According to the researchers, there are four criteria for a social factor to be a fundamental cause of disease;1) it influences multiple conditions 2) it is linked to various risk

factors, 3) the effects are reproduced over time, and 4) access to the social factor minimizes risk (Link & Phelan, 2010). Social capital theory postulates that social participation influences disease, through subjective components, such as social support being a buffer to stress, or through structural components, like welfare assistance, law enforcement, and emergency support (Cockerham et al., 2017). Social groups are also crucial as group participation changes health behaviors. Samuel et al. (2014), using the social capital model, found that people were less likely to engage in disease-promoting behaviors if they had trust in community members advocating for health behaviors. Finally, the health lifestyle theory proposes that healthy lifestyle behaviors cluster around social groups, such as class, race, and other social identifiers (Cockerham et al., 2017). Therefore, individuals choose a certain health behavior by the amount that a specific health behavior maybe more or less characteristic of their social groups, which may increase the risk of disease in particular communities.

Collectively, these four theories highlight the complexity that the SDOH literature tries to address between disease etiology and the social environment. When discussing the role of the SDOH on disease outcomes, research often studies the progression of a specific disease. This can make it challenging to find unifying theories, as studies often are situated within distinct social identities that may affect the literature addressed in that study. However, a few significant theories seem to support the relationship between SDOH and disease outcomes. The first theory is called the dose-response relationship (Penman-Arguilar et al., 2016). First employed in the study of toxicology, the dose-response model explains a cause-effect relationship in which a response is caused by a certain amount of exposure to a dose of a stimulus or stressor over time (Bolger & Carrington, 2005). When employed in SDOH research, the "dose" is an SDOH, and health outcomes are the "response" to the amount of exposure you have to that SDOH (Penman-

Arugilar et al., 2016). In other words, when an individual or social group has a deficit in an SDOH, future health outcomes are lower. In contrast, individuals with a sufficient amount of that SDOH generally have better health outcomes. This effect is magnified when looking at multiple SDOH and health outcomes across the lifespan. The second theory is called the "upstream SDOH." Upstream SDOH is a macro-level approach to understanding how socio-structural systems influence multifactorial causal chains of social factors (e.g., SDOH) that explain health outcomes (Bharmel et al., 2015). Upstream causes, such as government policy and health systems, affect SDOH across specific communities, affecting health outcomes in that group (Bharmel et al., 2015).

When discussing if SDOH influences immunological health in MLWH, it is important to look at multiple factors. As a disease with a social component in its etiology, it seems like progression research would be missing information if one did not examine HIV outcomes through a similar social theory lens. Many MLWH come from socially disadvantaged groups that already have a deficit in vital SDOH; thus, putting them at higher risk for worse immunological health outcomes. When considering the upstream SDOH, the historical issues between governmental structures and MLWH likely influence individual viral load and CD4 health in this population.

The significance on the SDOH was magnified in 2009 when the World Health Organization announced an initiative to increase knowledge and create commissions on the SDOH to decrease health inequalities around the world (WHO, 2009). The initiate included targeting specific diseases with the largest disparities, including HIV (WHO, 2009). Since this WHO initiative, there has been increased attention on the relationship between SDOH and complex diseases (Taylor et al., 2016). As HIV has a strong biopsychosocial component within

its etiology, it seems highly relevant that social factors, like the SDOHs, have influence on its progression and outcomes. The SDOH encompass five major categories; built environment, healthcare, social context, education, and economic stability, with different social factors placed into the five categories (WHO, 2009).

Social Factors of Social Determinants of Health

Built Environment.

The Built Environment category of the SDOH includes factors related to the relationship between social inequalities, the physical environment in which people live, and health outcomes (Shulz & Northridge, 2004). These factors include the physical (housing access, zip code, transportation) and natural environment (parks, sidewalks) (Kaiser Foundation, 2018; Shulz & Northridge, 2004). Researchers in built environments, such as urban planning, have long understood the community's role in preventing or exacerbating diseases (Pintar-Wollman & Jelic & Wells, 2018). The built environment can affect health outcomes in direct and indirect ways (Miller, 2017). Direct methods include access to the natural environment. For example, a cross-sectional study by Reuben et al. (2020) found that children without access to parks were more likely to be labeled as obese and diagnosed with ADHD than children with easy park access. Indirect methods include aspects of the environment such as zip code (Long et al., 2018). For instance, in the United States, mortality rates tend to be higher in rural areas than in urban areas (Long et al., 2018). Factors found to increase mortality rates in rural areas include; older populations, lack of transportation, and inadequate housing (Molinksy & Forsyth, 2018).

In the HIV literature, the built environment is also considered a crucial element in the disease's contractability. Pankhurst (2014) described how environmental structural and meditational

factors both influence HIV-risk in communities. Structural factors, such as poverty and homelessness, have been directly associated with higher HIV risk (Aidala et al., 2018; Pellowski et al., 2013). Mediational factors are mechanisms in the built environment that generate a "downstream" effect on a person's risk, such as food insecurity leading to engagement in sex-work (Parkhurst, 2014). Structural and mediational factors do not only affect people at risk for HIV. Similar to the general population, people living with HIV in rural areas face many indirect effects. Individuals living with HIV in rural areas have more barriers to care, including less access to appropriate medical services and unreliable transportation than individuals living in urban cities (Lahey et al., 2007). Although more likely to be closer to medical treatment, patients in urban environments are less likely to have insurance than their rural counterparts (Lahey et al., 2007). These barriers may result in the later initiation of antiretroviral therapy (Ohl et al., 2010). Evidence suggests that delay in treatment leads to higher viral loads and mortality rates (Ohl et al., 2010). According to one meta-analysis (Lahey et al., 2007), rural residents have higher mortality rates than urban residents, even when adjusting for age, race, and gender identity (Lahey, 2007). Thus, this research suggests that it is plausible that MLWH who live in urban environments may have lower viral loads and higher CD4 counts compared to individuals living in rural areas.

Health Care.

The factors contributing to the SDOH of health care include insurance access, quality of medical care, medical availability, and provider cultural competency (Kaiser Foundation, 2018). Access to health care has long been a complicated topic in the United States. *Access* is defined by the degree to which individuals can obtain services from the medical care system (Millman, 1993). In this country, access to healthcare, or medical availability, is often connected in the

research to insurance access. Studies indicate that uninsured adults are less likely to have access to preventative care and are more likely to suffer from chronic illness (Tolbert & Orgera, 2020). In 2019, three out of 10 uninsured adults delayed care due to costs (Tolbert & Orgera, 2020). These inequities also exist amongst people with specific diseases. An article by Casagrande & Cowie found that adults with diabetes without insurance were less likely to have regular check-ups, more diabetic complications, and high glucose levels (2012). Critically, people without insurance are more likely to die prematurely compared to people who have insurance (McWilliams, 2009).

Historically, gaining insurance was withheld from the HIV community until the late-2000s, as the chronic disease was considered a preexisting condition that left millions of PLWH uninsured (Raifman et al., 2019). Early research indicated that the lack of insurance access, thus little access to healthcare services, was correlated to higher mortality rates in the HIV affected community from the 1900s into the early 2000s (Goldman et al., 2001). A 2019 study analyzing 12 HIV adult care sites suggested that individuals with private or government insurance (Medicaid) had more consistent viral loads than patients who did not have insurance (Raifman, 2019). Despite the understanding that having insurance increases access to care and decreases viral loads, PLWH in parts of the U.S., particularly the Southern states, continue to experience barriers to gaining insurance. Adimora et al. (2014) studied 17 states and D.C. in the South to understand the impact of health insurance barriers on the HIV population. The research found that PLWH in the South are less likely to start antiretrovirals after initial diagnosis due to lack of healthcare coverage (Adimora et al., 2014). Furthermore, white and non-white patients report lower health outcomes, including lack of viral suppression and a lower quality of life (Adimora et al., 2014). Based on the research linking healthcare to HIV outcomes, it is reasonable to expect

that having access to insurance may likely contribute to lower viral loads and higher CD4 in MLWH.

Social Context.

The social context determinant encompasses social integration, social support, social stress, and community engagement that contribute to quality of life (Kaiser Foundation, 2018). As a multifaceted theory, social support is defined as information or actions of others' that lead an individual to feel secure and fosters feelings of communication and mutual obligation in a social community (Hupcey, 1998). Social support has been associated with regulating negative thoughts, promoting a sense of meaning of life, and facilitating health behaviors (Tough et al., 2017). Research has shown that social support is a preventative factor for mental health outcomes in ill patients. A study of 168 individuals with cancer showed a positive correlation between social support and perceived quality of life (Applebaum, 2014). Social support is equally important in chronic conditions. A meta-analysis indicated that social support was associated with mental health outcomes in people with disabilities (Tough et al., 2007). Integration and support of a social community can be crucial for individuals living with HIV when considering the high levels of stigma associated with the disease (Turan, 2017).

For example, a meta-analysis exploring 49 articles studying the quality-of-life outcomes in PLWH found that individuals with reported social support contributed to higher perceived quality of life outcomes across demographics (Degroote et al., 2014). Similarly, there is evidence of a connection between social support and medication adherence to antiretroviral therapy. Evidence indicates that social support can be either support or a discourage engagement in treatment, influencing viral loads (Gant et al., 2012). The experience of feeling included in a

community can increase the possibility of an individual with HIV participating in health-promoting behaviors, such as maintaining immunological health, to continue to take part in their social group (Smith, 2007). As such, MLWH who are socially active may see better viral health outcomes compared to others with little to no social activity.

Education.

As an SDOH, education includes literacy, early childhood education, vocational training, and higher education (Kaiser Foundation, 2018). Researchers often consider education as a *process* and a *product* (Hahn & Truman, 2015). As a process, education instills skills such as reasoning, self-efficacy, and values that evolve (Hahn & Truman, 2015).). For example, a study following 615 patients with diabetes found an association between education level, diabetes knowledge, and health outcomes (Walker et al., 2014). As a product, education provides skills and capacities that are related to social capital. Public health researchers have associated higher education as a "gateway" out of poverty and higher social position (Cohen et al., 2010).

Similarly, education plays a role in prevention and maintenance care in the HIV population. Ziegler and Stein (2015) found that education level as an SDOH played a significant explanatory role in HIV incidence rates across the United States. Education level can also influence health literacy or the degree to which someone can process health information. A literature review researching health literacy and PLWH found that lower levels of health literacy were correlated with lower medication adherence, elevated viral loads, and decreased CD4 counts (Reynolds et al., 2019). Due to the importance of education on viral health, it is reasonable to suggest that MLWH who have acquired education may have lower viral loads and higher CD4 counts.

Economic Stability.

Economic Stability as an SDOH consists of factors relating to income level, employment, debt, and living expenses (Kaiser Foundation, 2018). Income level has been a topic of public health interest as a considerable influence on health outcomes. According to researchers, the impacts of socioeconomic status (SES) begin at an early age. A meta-analysis by Cohen et al. (2010) found multiple studies indicating that lower socioeconomic status (SES) in childhood was a risk factor for premature death, despite the SES in adulthood. The analysis concludes that children of lower SES families have a higher chance of environmental exposures that becomes a pathway to worse health outcomes in the future. The association between SES and premature immature is inverse when considering children from higher SES families. The effects of SES do not stop at childhood. A study conducted between 1999-2016 found that cardiovascular disease was more prevalent in the lowest-earning group than the highest-earning groups (Abdalla et al., 2020). Higher incomes are generally associated with more health behaviors, resulting in higher life expectancy than people in lower-income levels (Chetty et al., 2016).

There is research indicating that income affects the HIV community. An analysis examining HIV diagnosis rates in 2006-2008 saw a positive correlation between HIV infection and income inequality (Gant et al., 2012). Disparities in outcomes also are indicated within different income levels between patients in active HIV therapy. In 2005 analysis of over 2,000 people with HIV showed that lower-incomes was one mediating factor for higher mortality rates (Cunningham et al., 2005). Other studies study income as a measure of perceived life outcomes in PLWH. A meta-analysis of PLWH found that income levels were negatively associated with perceived quality of life (Gisavand et al., 2020). At the lowest SES (e.g., poverty), income had a

degenerative effect on PLWH's quality of life over time (Gisavand et al., 2020). Thus, it is possible that having income can have an effect on viral health for MLWH.

Chronic Conditions

Along with exploring social factors related to health outcomes, researchers have begun to explore how other types of chronic illnesses may influence health outcomes for MLWH. According to the CDC, chronic illness is broadly defined by conditions that one year or more and require ongoing medical attention and affect daily living (2021). The literature suggests that chronic illness consequences are numerous, with patients suffering long-term psychological, economic, and social effects (Beatty & Joffe, 2206; Megari, 2013). It is estimated that around 6 out of 10 Americans live with a chronic illness (CDC,2021). As one chronic condition progresses, the vulnerability to other chronic conditions becomes more significant, a process known as a "synergistic interaction" (Singer et al., 2017). Synergistic interactions explain how one or more diseases affect the overall disease burden (Singer et al., 2017). The process is part of a larger theory called the syndemic model of health, which emphasizes the clustering of biological and social diseases within socially disadvantaged groups (Singer, 2020). The effects of synergistic interaction have far-reaching consequences, including; the rapid increase in disease progression, worsening symptoms, and decreased treatment efficacies (Singer et al., 2017). As HIV is a disease that weakens the body’s immune system, PLWH are more susceptible to other chronic illnesses (Yun-Yang et al., 2019). A study conducted in 2013 found that 94% of PLWH have chronic illnesses in addition to their positive status (Balderson et al., 2013). The effects of multiple chronic conditions have lasting effects on immunological suppression (Yun-Yang et al., 2019). For this study's scope, the paper will focus on chronic illnesses in three main areas; physical conditions, mental health, and chronic pain.

Physical Conditions.

PLWH are at risk for chronic physical conditions across the body through damage to the tissues, organs, and brain (Lucus & Nelson, 2014). There are few key reasons for this risk. First, the virus attacks the T-cells of the body. T-cells are the "fighter cells" of the immune system that attacks foreign antigens in the body (Lucus & Nelson, 2014). However, as the T-cells have to counteract the virus, the cells begin to dysregulate, a phenomenon known as "T-cell exhaustion" (Fenwick et al., 2019). This "exhaustion" results in sub-optimal immune levels that eventually lead even higher vulnerability to multiple chronic physical conditions (Fenwick et al., 2019). Another reason PLWH are at higher risk is potentially due to long-term antiretrovirals treatment. Despite the success of antiretrovirals, studies have indicated that the medication can cause drug-induced inflammatory responses that can place patients at greater risk for developing physical chronic illnesses (Nduka et al., 2016). For example, a 2018 meta-analysis found that PLWH on antiretrovirals had a fourfold increase risk in developing Type-II Diabetes due to drug-induced insulin resistance (Noubissi et al., 2018). Other studies have shown similar influence on antiretrovirals on blood pressure and hypertension in PLWH (Nduka et al., 2016). Lastly, the significance of traditional risk-factors, such as substance use, also places PLWH at a higher risk factor for chronic physical conditions (e.g., Hep-C) (Deeks et al., 2013).

Chronic physical conditions have long-term effects in PLWH. The symptoms of multiple physical conditions in PLWH include energy loss, sexual dysfunction, and changes in bodily appearance (Lazarus et al., 2016). These symptoms can greatly influence quality of life across domains for PLWH (Balderson et al., 2013). One of the first consequences of chronic physical conditions is premature aging, such as increased frailty (Desquilbet et al., 2007). This frailty has been linked to cognitive impairment and physical immobility (Desquilbet et al., 2007). Chronic

physical illnesses do not only affect the body. A study of aging individual with HIV found that, despite moderate levels of life satisfaction, symptoms of depression and stress, was associated with chronic disease burden (Balderson et al., 2013). Currently, research into the influence of physical conditions on viral suppression is a substantial gap in the current HIV literature. However, as the HIV population advances into old-age like never before, and chronic physical illnesses become more common, it is likely more studies will begin to look at the effects of these conditions on viral suppression. As prior research suggests, MLWH with physical chronic conditions may have higher viral loads and lower CD4 counts.

Mental Health Conditions.

The research literature has long associated HIV infection with a range of mental health conditions (Buckingham et al., 2013). According to some estimates, almost half of all PLWH have one or more psychiatric disorders (Yehia et al., 2015). Traditional studies between HIV and mental health conditions have mainly focused on psychiatric disorders; however, the rise of the opioid epidemic has sparked an interest in the co-morbidity of HIV, mental health disorders, and substance use disorders (Durvascula et al., 2014). For instance, 10- 28% of PLWH have co-occurring substance use and mental health diagnoses (Chandler et al., 2006). Intersecting factors influence the high prevalence of mental health conditions in PLWH. Individuals with mental health conditions often face psychosocial pressures (i.e., housing insecurity, food scarcity, environmental violence) contributing to a lack of adherence or access to HIV prevention tools (Chida & Vedhara, 2009; Remien et al., 2019). After diagnosis, the psychological stress of being HIV positive can further exacerbate the effects of prior psychological disorders, particularly Post Traumatic Stress Disorder (Remien et al., 2019). Patients may also have to choose between different care specialists if they cannot find a doctor who can adequately integrate their dual

diagnosis (Aggarwal et al., 2019). Other patient barriers to medical care include cognitive and social deficits caused by psychological disorders (Chander et al., 2006). Furthermore, social stigma presents additional challenges for the mental health of this population. HIV continues to be a highly stigmatized disease that disproportionally affects individuals who already face other discrimination, such as people of color, LGBTQ+ people, sex workers, and people who inject drugs (Remien et al., 2019). Long-term stigma have negative consequences on mental health disorders and overall quality of life (Remien et al., 2019).

Mental health conditions have significant effects on HIV care and outcomes. PLWH with preexisting mental health conditions are less likely to remain in HIV care after initial diagnosis (Chida & Vedhera, 2009). Poor retention in care is associated with a delay in starting antiretrovirals, non-adherence, and drug resistance over time (Chida & Vedhera, 2009). Mood disorders (i.e., depression, anxiety, Bipolar) are associated with a decreased likelihood of adherence and viral suppression (Merlin et al., 2012; Yeida et al., 2015). A study following 730 PLWH in Philadelphia found that the patients with a mental health diagnosis were less likely to achieve viral suppression after 12 months (Yedia et al., 2015). A meta-analysis by Chander et al. (2006) cited long-term studies that indicated that depression was connected to a decline in CD4 and viral load increases. There is a positive association between substance use disorder and the severity of HIV infection (e.g., AIDS status) (Coviello et al., 2018).

Other evidence that mental health disorders influence HIV outcomes is the research on mental health care treatment in HIV populations. A retrospective analysis found that individuals with HIV and one or more psychiatric conditions seeking mental health services had increased retention care rates than the group that was not receiving mental health services (Saag et al., 2018). Similarly, an analysis of 521 dually diagnosed participants (HIV and mental health

condition) at a clinic with integrated mental services found that individuals engaged in psychological services had higher adherence and viral suppression at baseline and 3-month follow-up compared to the non-engaged group (Coyle et al., 2019). These studies strengthen previous theories that attention to mental health conditions leads to better health outcomes for PLWH. Therefore, there is evidence to suggest that the presence of chronic mental health disorders can have a negative effect on viral suppression and CD4 counts in MLWH.

Chronic Pain.

Chronic pain is defined as the pain that persists past normal healing time that lasts more than 3-6 months (Treedee et al., 2016). In 2016, 50 million U.S. citizens reported dealing with a type of chronic pain condition (Dahlhamer et al., 2016). Among PLWH, the prevalence of chronic pain is higher, with some estimates around 50% to almost 83% (Baker et al., 2020). Analyses indicate that pain reported by PLWH is ten times more likely to result in functional impairment (Merlin et al., 2013). Similar to the other chronic conditions discussed above, PLWH have multiple biological mechanisms that increase the risk of experiencing chronic pain. For instance, inflammation of the immune system's peripheral cells, monocytes responsible for clearing pathogens, is often an adaptive response to HIV infection (Addis et al., 2020). However, as HIV progresses, the peripheral cells begin to generalize and attack healthy cells, leading to increased hypersensitivity to pain (Madden et al., 2020). This hypersensitivity is often associated with the beginning stages of HIV-related peripheral neuropathy, which can then spread across the body (Addis et al., 2020). Antiretrovirals similarly place PLWH at higher risk for experiencing chronic pain. Long-term use of the medication is associated with neurotoxicity developed when the antiretrovirals contact HIV infection proteins that affect cells (Philips et al., 2010). The result of

these interactions can lead to peripheral neuropathy and widespread chronic pain. Chronic pain has a variety of health outcomes for PLWH.

Research has found that chronic pain is associated with higher viral loads and lower CD4 counts in PLWH (Addis et al., 2020). This finding has an impact on long-term viral suppression. A study conducted on PLWH in south Florida found that only 42% of individuals with chronic pain achieved viral suppression compared to 61% of individuals with no chronic pain (Surrat et al., 2015). A one-year longitudinal study by Merlin et al. (2018) followed over 2,000 PLWH with chronic pain from 2015 to 2016. The results found that individuals with chronic pain were more likely to miss routine care visits and had higher immunological failure rates (higher viral loads/lower CD4) the subsequent year (Merlin et al., 2018). Other studies found that immunological health could also influence the perception of pain. A cohort study of individuals with HIV found that participants with detectable viral loads (<50) had lower pain thresholds and tolerance, suggesting that higher viral loads may be associated with more pain sensitivity (Goodin et al., 2017). The primary treatment for chronic pain in PLWH continues to be opioid therapy (Merlin et al., 2018). However, studies analyzing the effects of long-term opioid treatment have not found a decrease in viral suppression amongst PLWH taking opioids (Joseph et al., 2020). Although the literature has not found evidence that opioids affect HIV immunological outcomes, the risks for dependence may be higher considering the risk factors for substance use in this population (Madden et al., 2020). The additive effect of chronic pain and mental health condition, like substance use disorders, further indicates the need to understand the role of these chronic conditions in the health outcomes for PLWH. As chronic pain research has shown effects on HIV outcomes, it is reasonable to suggest that MLWH with chronic pain may have lower viral loads and CD4 counts compared to MLWH that do not have chronic pain.

THE PRESENT STUDY

The current research literature has started to consider how SDOH and other chronic conditions affect health outcomes in the HIV community. SDOH has become a topic of increasing interest in understanding complex illnesses like HIV and analyzing how the presence or absence of these social factors influence viral health. Similarly, the literature finds that chronic conditions associated with HIV have many short and long-term effects on health outcomes. Few studies are addressing the effects of both of these variables on viral load and CD4 variance. This study examined how SDOH and chronic conditions, individually and collectively, affect the viral load and CD4 count in MLWH. Based on the theory and research literature, it was hypothesized that MLWH who possess any single SDOH would have a lower average viral/ higher CD4 counts than individuals possessing no SDOH (H_1). In addition, it was hypothesized that MLWH with one or more chronic conditions would have higher (worse) viral loads and lower CD4 counts compared to the men with no chronic conditions (H_2). Lastly, the combination of SDOH and chronic conditions would explain more of the variance in viral load and CD4 variance over SDOH or chronic condition individually in MLWH (H_3).

CHAPTER THREE: METHOD

Procedures

As the study designed involved using secondary data, the procedures for the study generally match those described in Bierma (2019). Namely, information on participants was reported through retroactive data collection of participant medical files. Baseline intake information included variables, such as; demographic information, HIV transmission history, viral load/CD4 counts, chronic health condition history, and substance abuse history. The information in the medical file was self-report which prevented further understanding of duration or severity of the variables collected. The current study evaluated the original database for SDOH and chronic condition variables. Particular variables were later analyzed as continuous measure for further analysis.

Participants

Participants included 130 MLWH who received services from Positively Living from 2012-2018. Positively Living is a non-profit that serves individuals living with HIV in 11 counties in east Tennessee with food, medical, and housing assistance. This data was originally collected as part of a dissertation project completed by Dr. Shane Bierma to examine antiretroviral adherence (Bierma, 2019). As the original raw demographic information was not available at the time of analysis, participant demographic information was obtained from Dr. Bierma's original dissertation manuscript. As the study did not use all participants described in Dr. Bierma's dissertation (130 versus 133), it is important to note that the demographic averages may not reflect this study's true demographic averages. According to the information provided the dissertation, the sample's mean age was 46.5 years old (range = 22-68 years old, SD = 11.32; Bierma, 2019). All participants identified as male in the sample. The self-reported ethnic

background of participants was predominately White, non-Latino (63%), or African American (31%). Other participants identified as Latino (5%) or Native American (1%) (Bierma, 2019). Individual transmission of HIV was reported as same-sex contact (N = 72); different-sex contact (N = 43); unknown method (N = 13); IV drug use (N = 2); tattoo (N = 2); and dental work (N = 1) (Bierma, 2019). Other demographic information included religious preferences; Christian (N=31), Baptist (N=25), Atheist/none (N=47), and other (N=27).

Measures

Social Determinants of Health

Built Environment.

The built environment variable was analyzed by differentiating urban versus rural zip codes. Zip codes outside of Knox County (biggest metropolitan city) were categorized as "rural," and zip codes within Knox county were categorized as "urban."

Health Care.

Health care was categorized based on the presence or absence of insurance (No/Yes).

Social Context.

Social context was analyzed by social activity in which participants were asked whether they would describe themselves as socially active (No/Yes). Self-report of social activity was later documented as not socially active or socially active (No/Yes).

Education.

Education was defined by level of education ascertained by participants. First, participants were categorized by either less than a high school diploma or high school diploma/ greater degree. A partial continuous scale of education (i.e., no high school diploma; high school diploma; higher degree) was employed for exploratory analysis (described below).

Economic Stability.

Economic stability was determined by participant self-report if they receive monthly income (yes/no). A continuous variable of monthly income was measured by determining the sample median income for exploratory analyses (described below). Monthly income was categorized as either low for individuals who fell under the median income ($863) and high for individuals who fell above the median income.

Chronic Conditions

Physical Conditions.

Physical conditions were defined by participant self-reported non-communicable diseases (i.e., cardiovascular disease, cancer), specific degenerative diseases (i.e., autoimmune, joint disorders), communicable diseases (i.e., Hepatitis C), specific organ disease (i.e., organ failure) and/or neurological disease. A total count of each physical condition was calculated for each participant and was treated as continuous variables for exploratory analysis.

Mental Health Conditions.

Mental health conditions were identified by participant self-reports of mental health disorders and/or substance use disorders. The continuous mental health conditions variable was later defined by the number mental health conditions reported by each participant to use for exploratory analysis.

Chronic Pain.

Chronic pain was defined by participant self-reports of chronic pain and/or neuropathy in specific or general areas of the body (Yes/No).

Data Analytic Plan

All statistical analyses were assessed utilizing SPSS Statistics 27 (IBM, 2020). Conducting early analysis of the data indicated that viral load and CD4 were positively-skewed; thus, a log-transformed was used to meet normality assumptions. The initial analyses measured frequency, means, and standard deviation of the study's variables. Bivariate correlations were calculated to initially measure the relationship between study variables. Hypothesis 1 was analyzed using independent t-tests to determine the mean difference of viral load and CD4 count for each dichotomous variable of the SDOH. Hypothesis 2 used independent t-test to study the mean difference of viral load and CD4 count for each chronic condition.

To test hypothesis 3, multiple regression models were used to understand the variance in viral load and CD4 counts. In the first two regression models, SDOH and chronic conditions were analyzed separately to find whether the factors individually contributed to variance in the outcome variables. The third regression model created featured both SDOH and chronic conditions to understand the extent in which the variables together explain the variance in viral load and CD4 counts. Please see below for explanation and results of the exploratory analysis with the data.

CHAPTER FOUR: RESULTS

DESCRIPTIVE STATISTICS

Analyses included 130 men living with HIV. Initial descriptive statistics indicated that mean viral load and CD4 count for the sample were 17650.95 (*SD*= 65,520.3) and 638.47 (*SD*= 487.18), respectively. The sample was comprised primary of men living in an urban area (73.1%) with a high school or greater degree (74.6%). A little more than half of the sample had insurance (60%), but did not have income (50.8%), and about half reported being socially active (51.5%). According to the analysis, most men reported no current physical chronic conditions (60%), whereas a similar number reported having a chronic mental health condition (57.7%). Lastly, the majority of men did not report any chronic pain (83.3%). Pearson correlation analysis for each variable and viral load/CD4 are reported in Table 1. As Table 1 indicates, insurance ($R(128) = -.319, p<.001$), and chronic pain ($R(128)= -.173$, $p=.049$) were both negative correlated with viral load; whereas, socially active ($R(128)=.118$, $p=.032$) was positively correlated with viral load. Information on SDOH ranges for the sample are reported in Table 2.

Hypothesis 1.

Hypothesis 1 proposed that MLWH who possess any single SDOH would have a lower viral load and higher CD4 count compared to the men not possessing that SDOH. Results suggest that hypothesis 1 was partially supported. Similar to research on social context, individuals who were socially active were seen to have a lower viral load compared to the men who were not socially active ($t(128)=-2.14$, $p=.001$). Interestingly, The results did show that men with insurance had a higher mean viral load compared to men without insurance ($t(128) = 3.21$, $p= .001$), which is contrary to the health care research that would suggest men with insurance would have lower mean viral loads. Similarly, men with monthly income had a higher viral load

compared to men with no monthly income ($t(128)= 1.64$, $p=.02$). There was no significant mean difference in viral load for education or county (see Table 3 for Viral Load results). Lastly, there was no significant mean difference in CD4 count between men who possess SDOH or men who possess no SDOH (see Table 4 for CD4 results).

Hypothesis 2.

Hypothesis 2 proposed that men with one or more chronic conditions would have lower viral load and higher CD4 counts compared to men who do not have chronic conditions. Results suggest that this hypothesis was also partially supported (see Table 5 for Viral Load results). Findings indicate that there was a significant mean difference in viral load for men with chronic pain compared to men with no chronic pain ($t(128)=1.99$, $p=.001$). In comparison, there was no significant mean difference between viral loads for men with physical chronic conditions compare to men with no chronic conditions ($t(128)=.13$, $p=.58$), which is not consistent with research findings. Additionally, the results suggested that the trend was similar for mental health conditions ($t(128)= .-59$, $p=.59$). Again, there was no significant difference in mean CD4 counts for men with or without chronic conditions (see Table 6 for CD4 results).

Hypothesis 3.

Hypothesis 3 proposed that the combination of SDOH and chronic conditions would explain significantly greater variance in viral load and CD4 variance over SDOH or chronic conditions individually. Results indicated that this hypothesis was not supported (see Table 7 for Viral Load results). The multiple regression model for SDOH indicated that the variables explained 15% of the variance in viral load in the sample ($F(5,124) = 4.127$, $p>.001$), $R^2=.145$). However, when utilizing hierarchical regression to examine whether the R^2 change was significant, there was no significant change to the model. Chronic conditions did not

significantly explain the variance in viral load ((3,126) =1.533, p=.21), R^2=.04). The model including both groups indicated that 19% of viral load variance in the sample compared to the variables separately (F(8,121) =3.49, p=.004), R^2=.19). However, further hierarchical analysis found that the R^2 change was not significant. Following the trend of earlier analyses, no models were significant in explaining the variance in CD4 in the sample (see Table 8 for CD4 results).

Exploratory Analysis.

As the initial results did not provide substantial evidence for the study's hypotheses, it was deemed necessary to examine further analysis to clarify the research questions. Subsequent analyses focused on the effect of the dose-response model. As such, the exploratory analyses considered the impact that continuous variables of SDOH and chronic conditions (i.e., more 'doses') had on viral load and CD4 variance, rather than simply the presence or absence of each variable.

As the literature emphasized the importance of higher income and education on immunological health outcomes, it was deemed appropriate to analyze whether varying levels of monthly income and education level would have an effect on viral load and CD4. One-way ANOVA was used to identify if mean viral load and CD4 count changed based on numeric monthly income among participants The results of the ANOVA determining if mean viral load and CD4 changed based on participants numeric monthly income was not significant (F(2, 127)=1.28, p=.282); F(2,127)= 1.04, p=.36, respectively). Bivariate correlations were utilized to determine if varying levels of education (see above) were related with viral load and CD4 count. Similar to income, bivariate correlation of the relationship between varying levels of education and viral load and CD4 count was also not significant (R(130)=-.87, p=.33); R(130)=-.87, p=.30, respectively).

As having more than one chronic condition is considered a significant stressor on immunological health, the number of physical and mental health conditions reported by participants was indicated. Bivariate correlation found that the relationship between continuous chronic physical conditions ($R(130)= -.04$, $p= .63$); $R(130)= -.86$, $p= .33$, respectively) and mental health conditions ($R(130)= -.20$, p= .83; R(130)= .04, p= .66, respectively) were not significant for viral/CD4 count. Within the multiple regression models, additional models were created using the continuous SDOH and chronic condition variables to find if levels or amounts of certain variables had an effect on the multiple regression models analyzing variance in viral load and CD4 count. A multiple regression model replacing continuous SDOH (income and education) and chronic conditions was found to be significant in explaining the variance in viral load ($F(8,123) =3.255$ $p=.002$, $R^2=.18$) but not CD4 ($F(8,121) =.62$, $p= 76$, $R^2=.04$). The model analyzing the SDOH and continuous chronic conditions was significant for viral load variance ($F(8,121) =2.93$, $p=.005$, $R^2=.16$) but not significant for CD4 ($F(8,121) =.36$, $p=36$, $R^2=.023$). Multiple Regression model using continuous SDOH variables and chronic conditions was similarly significant for explaining variance in viral load ($F(8,121) =2.67$, $p=.010$, $R^2=.15$) but not significant for the explaining the variance of CD4 ($F(8,121) =.613$, $p=.77$, $R^2=.04$).

CHAPTER FIVE: DISCUSSION

Human Immunodeficiency Virus (HIV) continues to be a significant issue amongst the most vulnerable in our society (AVERT, 2019). Immunological health and viral suppression continue to be the most effective way for people living with HIV (PLWH) to maintain a healthy quality of life and prevent the virus's spread (Sax, 2012). Traditional HIV research has mainly focused on individual health behaviors to understand viral load and CD4 variance in this population; however, this metric has not addressed all the factors that influence immunological health. Research into social factors, such as SDOH and the influence of chronic illness (physical, mental health, and chronic pain), has become increasingly common in HIV research literature. Despite the importance of these factors, little research has examined the individual and collective effects of these variables in the viral load and CD4 count variance in this population. The current study aimed to assess how SDOH and chronic illnesses effect the variance of viral load and CD4 in men living with HIV.

Hypothesis 1 assessed whether the presence or absence of SDOH influenced the mean difference of viral load and CD4 count in the sample. The findings partially supported the hypothesis; specifically, results found that men who were socially active had lower mean viral loads than men who were not socially active, which substantiated prior research. It is important to note that the measure of social activity was based on a self-report rating, meaning that it was more indicative of a participant's perceived levels of social activity. As such, it is difficult to determine the individual definition of social activity without being able to directly ask participants. However, it seems that, even when considering how a participant may define social activity for himself, it has a positive influence on mean viral load in the sample. However, there were surprising results for the outcome of income and insurance in the study. When following

the evidence of prior research, men in the sample with monthly income and insurance should have had lower mean viral loads than men with no insurance and income; yet, the results indicated that men with these SDOH had higher mean viral loads. These contractionary findings suggest that there are considerations not addressed in the hypothesis. For instance, despite having a monthly income, many men in the sample were on fixed incomes (e.g., SSI or SSDI), which often provides lower monthly stipends than full-time employment. When considering the dose-response theory, a small fixed income may not provide enough "dose" to adequately address an individual's monthly needs, causing more undue stress that in turn could pose greater risk for higher viral loads.

The higher mean viral loads for men with insurance suggest complex aspects of this determinant were not met by simply placing the sample into a dichotomous category (access versus non-access). One of these aspects could be *the quality* of healthcare, which is also a factor in the healthcare category (Allen-Duck et al., 2017). Quality of healthcare emphasizes the importance of provider cultural competence, evidence-based treatments, and preventative care for individuals accessing medical services (Allen-Duck et al., 2017). For example, if the participants in this study's sample had insurance, but their doctor stigmatizes them or gives them outdated HIV treatment, these factors could potentially cause an individual to delay treatment that could affect viral load variance over time.

Lastly, the mean variances in CD4 count were not supported by hypothesis 1. There could be many explanations on why SDOH may not influence CD4 count. First, CD4 count may be less susceptible to environmental influences than viral load. Another relevant factor is the changing aspects of living with HIV. As noted earlier, antiretrovirals have allowed PLWH to live healthier lives with the virus than ever before. For example, many of the study's participants have strong

virological health (i.e., low viral loads/higher CD4 counts), which places them in a "maintenance stage" of this disease. This maintenance phase allows individuals not to see extreme variability in the CD4 counts as one might see in later stages of HIV (i.e., AIDS).

Hypothesis 2 assessed whether the absence or presence of chronic conditions (physical, mental, and chronic illness) influenced viral load and CD4 count variance. The results partially supported the hypothesis. The results found that men with chronic pain had higher viral loads than men with no chronic pain supported the evidence provided by past research. However, chronic physical and mental health conditions did not show any effect, which was unexpected when considering the literature on chronic conditions and HIV. One reason for this null effect is that participants may be underreporting physical and mental health conditions on baseline paperwork due to stigma-related concerns. Another possibility is that many study participants found the non-profit organization due to stressful life events, such as food insecurity or unstable housing. Thus, these acute stresses may have more of an effect on viral load and CD4 than chronic conditions at the time of intake.

Furthermore, a limitation of the mental health condition variable is that there was no differentiation made between mental health disorders and substance use disorders in the data. This lack of differentiation may have made it more difficult to parcel out if active substance use could have affected viral load and CD4 variance in the sample. Later analysis might benefit from distinguishing between these two groups for a clearer picture of how different psychiatric conditions affect virological health in PLWH. Similar to hypothesis 1, chronic conditions did not affect CD4 count. Again, this could respond to the disease phase represented in the sample that may not be as influenced by chronic conditions, particularly if these conditions are also in the maintenance phase.

Hypothesis 3 assessed if the combination of both SDOH and chronic conditions had an effect on viral load and CD4 variance. The results did not support the hypothesis. It is possible that there were other significant factors not explored that could have impacted on outcomes. One of those factors could be medical adherence to antiretrovirals. Although individual medical behaviors was outside the scope of the study, the effect of medical adherence on immunological health is a relevant factor along with SDOH and chronic conditions factor that needs to be addressed in future research.. Additionally, interactions amongst the study's variables could explain the variance in viral load and CD4 count. For example, interaction amongst factors, such as education and monthly income, may give a better picture on how these variables together influence viral load and CD4 variance.

Limitations

While the current study's strengths include how the research expands upon current literature to analyze how SDOH and chronic conditions collectively affect immunological health; however, there are notable limitations to this study. Overall, as the relationship between the variables are complex and often intersecting, it can be difficult to definitively identify the individual influence of these factors without missing important context from other variables, especially considering that this research was based on secondary data. Reliance on secondary data means that the current study was limited to the original information collected, which narrowed the scope of variables analyzed. Relatedly, information and context were missing due to the time between the studies. The time lapse also means that aspects of the sample's variables and demographics could have changed over time, which may have changed the study's outcomes.

A further limitation to the study is that the population sampling was limited to participants living in east Tennessee. This geographic restriction means that the data is limited in its

generalizability to PLWH in other geographical areas. Future research could benefit from comparing the influence of these variables in PLWH who live in different parts of the state and country. Additionally, as the participants were clients at a non-profit, it is possible that the majority of the participants already have significant deficits in resources highlighted by the SDOH, such as income, alluded to earlier. Thus, there is a restricted range in the variety of resources available for analysis that could skew results or limit the scope of findings.

Another limitation is the lack of knowledge about the participant's SDOH history. As the etiological theories suggested, early exposure to SDOH social factors during childhood often determines the present effect of these factors in someone's life. The lack of information regarding childhood SDOH means missing context on how the current state of the variables effect viral load and CD4 variance. Lastly, there is a limitation on the amount of current literature specifically discussing CD4 count variance in this population. As such, it was difficult to understand why the study's variables had no effect on CD4 or what other variables need to be addressed to understand the variance in this important immunological health marker.

FUTURE DIRECTIONS AND CLINICAL IMPLICAITONS

The study's results could give guidance to clinical interventions moving forward. For instance, as the study found that social activity can help support lower viral loads, clinicians should ask questions about a client's social support and possibly connect them to support groups or communities to help prevent social isolation. It will also be important for clinicians working with individuals with HIV to ask about chronic conditions, specifically chronic pain, to ensure that the patient is balancing their health care needs across their different conditions. It would be beneficial to conduct clinical assessments, not only about the presence of SDOH, but also the

quality of those resources and if they are truly meeting the needs of the individual. As the results suggested, just because a patient may have access to insurance or income, does not mean there may not be gaps to be addressed with additional community resources. Further understanding of how SDOH and chronic conditions affect immunological health in PLWH will assist clinicians to be more prepared to discuss and implement targeted interventions that alleviate the health inequities related to these factors.

Research should continue to address how variables like SDOH and chronic conditions affect viral load and CD4 variance in PLWH. As discussed previously, future research should consider the complexity amongst these variables and find avenues to investigate how to analyze the influence of a variable more specially. For example, future research could consider using these variables as moderators or mediators in the relationship between medical adherence and immunological health. Understanding how these variables may play a role in this relationship could help parcel out individual influence, as well as potentially introduce any indirect effects (e.g., moderated mediation or mediated moderation) that could not be found in this type of analysis. It might similarly be helpful to investigate how stress may play a role in viral load and CD4 count in PLWH. Expanding to other types of demographics (i.e., gender) or other geographic areas (i.e., west versus east TN.) could help examine how these variables affect immunological health for people with varying social identities, particularly marginalized identities. Furthermore, longitudinal research following SDOH and chronic conditions could help fill in gaps in the current literature on how these variables shape immunological health overtime for PLWH.

Conclusions

The current study investigated how SDOH and chronic conditions related to variance in viral load and CD4 variance in men living with HIV. Results indicated that social activity and chronic pain are both related to viral load variance (positively and negatively, respectively). Although other hypotheses were not supported, it is critical to continue to research how social factors and chronic illnesses affect viral load and CD4 count in PLWH. Information on these variables could help shape intervention strategies as PLWH begin to live longer with the disease. This study may add to emerging research on the relationship between SDOH and chronic conditions and immunological health. Future research should focus on following these variables over time and how varying levels effect quality of life for PLWH.

Compliance with Ethical Standards

All procedures involving human participants were performed in accordance with the ethical guidelines of the institutional research committee.

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