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Optimizing Viral Suppression Among People Living with HIV: A Comprehensive Exploration of Neighborhood Environments, Physiological Factors, and Quality of Life

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Optimizing Viral Suppression Among People Living with HIV: A Comprehensive Exploration of Neighborhood Environments, Physiological Factors, and Quality of Life

A dissertation submitted in partial satisfaction of the

requirement for the degree of Doctor of Philosophy

in Epidemiology

by

Roxana Rezai

2024

ABSTRACT OF THE DISSERTATION

Optimizing Viral Suppression Among People Living with HIV: A Comprehensive Exploration of Neighborhood Environments, Physiological Factors, and Quality of Life

by

Roxana Rezai

Doctor of Philosophy in Epidemiology

University of California, Los Angeles, 2024

Professor Sung-Jae Lee, Chair

The introduction of Antiretroviral Therapy (ART) in the late 1980s has transformed HIV from a fatal disease into a manageable chronic condition, although challenges like adherence to treatment and broader socio-economic factors continue to impact viral suppression and overall health status among people living with HIV (PLWH). The objective of this dissertation is to examine social (community environments), biological (pain), and psychological (self-perceived quality of life) factors associated with viral suppression among PLWH.

The first paper investigates the association between neighborhood and sociodemographic factors and viral suppression among PLWH in Southern California, focusing on areas served by Ryan White clinics. Contrary to expectations, higher walkability scores were associated with lower levels of viral suppression. In line with our hypotheses, longer commute times were negatively associated with viral suppression. Employment showed a positive association with

viral suppression, while higher poverty levels and longer work hours negatively impacted viral suppression rates. Additionally, no significant relationships were found between education level, public transportation score, and viral suppression.

Given that PLWH often report higher instances of pain and substance use compared to the general population, the second paper explores the association between pain and viral suppression and how substance use modifies this relationship. We found that there was no substantial association between pain and viral suppression among women living with HIV (WLWH) in our cohort. Furthermore, we saw no modification by any type of substance use.

The third paper examines the role of quality of life (QoL) on viral suppression and any disparities in this association by race/ethnicity. QoL, encompassing physical health, psychological well-being, and socioeconomic stability, has been consistently linked to viral suppression. We found a significant positive association between QoL and viral suppression (aOR: 1.17, 95% CI [1.10, 1.25]). However, the magnitude of this association was shown to vary by racial and ethnic group. The increase in odds of viral suppression per one-point rise in QoL score was greatest among White WLWH and least among Black WLWH.

Understanding the individual impact of each factor examined allows for the development of targeted, effective interventions. These findings not only advance our knowledge of HIV management but also emphasize the need for a multi-faceted approach that addresses the specific needs and circumstances of individuals living with HIV.

The dissertation of Roxana Rezai is approved.

Onyebuchi A. Arah

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University of California, Los Angeles
2024

DEDICATION

To my brother, my first and forever friend in life.
To my mom, my biggest cheerleader.
To my dad, my compass.

Table of Contents

LIST OF TABLES

LIST OF FIGURES

LIST OF ACRONYMS

Activities of daily living (ADL)

Acquired Immunodeficiency Syndrome (AIDS)

Adjusted Odds Ratio (aOR)

Antiretroviral Therapy (ART)

California (CA)

Centers for Disease Control and Prevention (CDC)

Center for Epidemiologic Studies Depression (CES-D)

Center for Neighborhood Technology (CNT)

Confidence Interval (CI)

Directed acyclic graphs (DAG)

Ending the HIV Epidemic (EHE) Human Immunodeficiency Virus (HIV)

Federal Poverty Level (FPL)

Highly Active Antiretroviral Therapy (HAART)

Health People Index (HPI)

High School (HS)

Intimate partner violence (IPV)

Implementation Science Coordination Initiative (ISCI)

Men who have sex with men (MSM)

Odds Ratio (OR)

People living with HIV (PLWH)

Post-Traumatic Stress Disorder (PTSD)

Pre-exposure prophylaxis (PrEP)

Quality of Life (QoL)

Sexually Transmitted Infections (STI)

Standard Deviation (SD)

Status neutral antiretroviral therapy (START)

Women living with HIV (WLWH)

Women's Interagency HIV Study (WIHS)

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VITA

Education

2024	Doctor of Philosophy Candidate, Epidemiology Fielding School of Public Health University of California, Los Angeles
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Chapter I. Introduction

Background

History & Prevalence of HIV in the U.S.

The history of Human Immunodeficiency Virus (HIV) in the United States traces back to the early 1980s, when clusters of previously healthy men who have sex with men (MSM) are suddenly admitted to the hospital for various opportunistic infections, cancers, and weakened immune functions, which will later be identified as Acquired Immunodeficiency Syndrome (AIDS).[1] Initially identified among MSM, the epidemic quickly grew to affect a diverse cross-section of the population, signaling a national and global health crisis.[2] Over the decades, concerted efforts in public health and research have led to significant advancements in understanding HIV transmission routes, treatment options, and prevention strategies. Despite these advances, HIV remains a critical public health issue in the U.S., with the Centers for Disease Control and Prevention (CDC) estimating approximately 1.2 million people living with HIV (PLWH) and over 35,000 new infections diagnosed in 2021 among individuals 13 years and older in the U.S.[3]

HIV Transmission Routes

HIV transmission in the U.S. primarily occurs through specific behaviors and exposure routes, with the primary modes of transmission including anal or vaginal sex and sharing needles, syringes, or other drug injection paraphernalia.[4] Bodily fluids such as blood and semen are able to transmit the HIV virus, and for transmission to take place, these bodily fluids need to encounter a mucous membrane or be directly introduced into the bloodstream via needles and syringes.[5] Given these transmission routes, we find that the largest number of new HIV diagnoses in the U.S. are attributed to male-to-male sexual contact, followed by heterosexual

contact, and injection drug use.[6] Globally, differing social, cultural, and economic contexts can influence these patterns, leading to different high-risk populations. For example, in Sub-Saharan Africa the main mode of transmission is due to heterosexual sex, making women an important group to target due to high rates of mother to child transmission,[7,8] while in Central and Eastern Europe injection drug use can be attributed as the leading cause of HIV among their residents.[9,10]

HIV by Sex

HIV affects individuals across all sexes, but epidemiological data reveal significant disparities in prevalence and outcomes. MSM continue to be the most heavily impacted group, accounting for a disproportionate number of new HIV diagnoses in the U.S.[3] However, women, also face unique challenges and risks regarding HIV transmission, progression, and treatment outcomes.[11] HIV rates among women have seen a slight decline in recent years, however certain sub-populations have seen either an increase or no change in number of new diagnoses, and despite these trends, women are underrepresented in both literature and HIV treatment/vaccine trials.[12,13] A published systematic review of HIV clinical trials reported that women accounted for only 19% of participants in HIV treatment studies and 38% of vaccine studies.[14] This underrepresentation is particularly concerning given that among individuals at risk or living with HIV, women are less likely to be taking pre-exposure prophylaxis (PrEP), an effective medication that prevents contraction of HIV, and less likely to be virally suppressed compared to their male counterparts.[15,16] According to a 2021 CDC HIV surveillance report, only 10% of women who would benefit from PrEP were prescribed PrEP in the U.S.[16]

HIV by Race/Ethnicity

When examining HIV incidence and prevalence rates by race and ethnicity, we find that Black/African Americans and Hispanic/Latinos are disproportionally affected compared to their

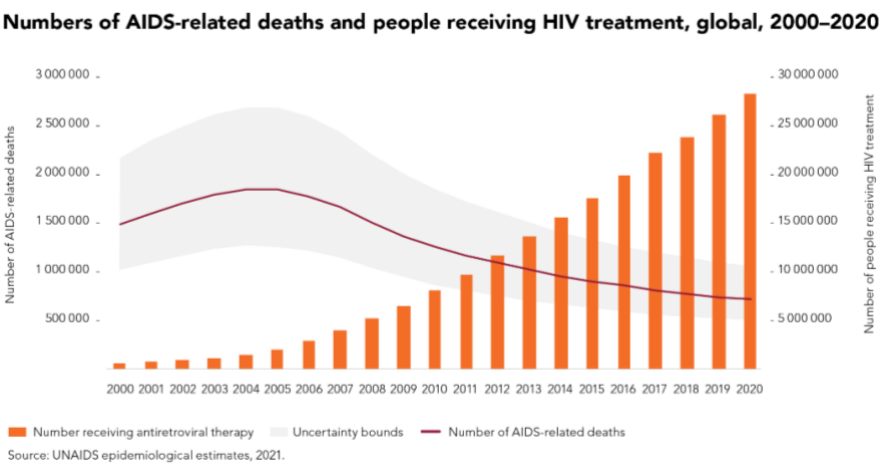
White counterparts. In 2021, despite representing only 12% of the U.S. population, Black/African Americans accounted for 40% of new HIV infections.[17,18] Similarly, Hispanic/Latinos, who constitute 18% of the population, disproportionately represent 29% of new infections.[17] When examining HIV prevalence rates, the CDC reports that Black/African Americans are 7 times more likely and Hispanic/Latinos are 3 times more likely to be living with HIV compared to White individuals.[18]

These disparities are not simply the result of individual behavior but reflect broader issues of structural and systemic inequities facing racial and ethnic minorities in the U.S.[19] Medical mistrust, structural racism, and cultural stigma have all been shown to impact access and utilization of HIV prevention and treatment services.[19-23] Unequal access to healthcare due to limited clinical resources in predominantly Black and Brown neighborhoods, housing instability, and discrimination within medical settings significantly hinder the ability of Black and Brown individuals living with HIV to access necessary services.[24-26] Addressing these inequities requires greater representation of racial and ethnic minorities in research as well as comprehensive public health responses, including culturally sensitive prevention, treatment, and support services.

HIV Treatment in the Age of ART

Since its development in the late 1980's, Antiretroviral Therapy (ART) has revolutionized the management of HIV, turning a once fatal diagnosis into a manageable chronic condition.[27]

ART utilizes a combination of antiretroviral drugs to suppress the virus to less than 200 copies of HIV per milliliter of blood, also known as viral suppression, preventing the progression of HIV to AIDS.[28] This breakthrough in HIV care has significantly altered the treatment landscape, making it possible for individuals with HIV to lead longer, healthier lives.[27] High adherence to ART regimens is a vital factor in maintaining viral suppression and preventing the development of drug resistance HIV strains.[29,30] Research suggests that adherence levels of 90%-95% are necessary to achieve viral suppression, yet numerous factors can impede this goal.[29]



Barriers and Facilitators to Viral Suppression

Factors influencing viral suppression among PLWH include socio-economic challenges, such as poverty and lack of access to healthcare;[31] psychological barriers, like depression or anxiety[32]; and community and neighborhood-level issues, such as lack of local healthcare facilities or poor transportation options.[33,34] Each of these factors individually can significantly impact viral suppression among PLWH, and the interplay between them can compound these effects, making the task of addressing them even more complex.[35]

Risk Factors at the Community/Organizational Level

Community and organizational level factors, such a neighborhood walkability and transportation options play a crucial role in either facilitating or hindering viral suppression

among PLWH.[36] High walkability scores, indicating ease of access to healthcare facilities, pharmacies, and support services for those without transportation can facilitate better ART adherence and increase rates of viral suppression.[37] Conversely, high levels of neighborhood violence may deter residents from accessing essential medical facilities, potentially leading to lower rates of viral suppression.[38] The CDC also highlights the impact of violence on community growth and strains on the medical system, where violence may lead to neighborhood isolation as businesses and health clinics relocate to neighborhoods with lower levels of community violence.[38,39]

Risk Factors at the Individual Level

Individual-level factors also play a crucial role in achieving viral suppression among PLWH. Research suggests that individuals experiencing mental health challenges, income instability, and housing insecurity often encounter barriers to adherence to ART which is essential for viral suppression.[40-42] Substance use has been associated with decreased engagement in HIV primary care visits and lower adherence to medication regimens, partially due to stigma.[43,44] Additionally, physiological challenges, such as experiencing severe pain, impact the ability to perform activities of daily living, further affecting engagement and adherence.[44,45]

Drug and alcohol use, a prevalent concern among PLWH, is associated with lower rates of medication adherence, contributing to virologic failure and increased mortality rates.[46] Although HIV inherently compromises the immune system, making it challenging for the body to combat infections and cancers, substance use exacerbates the impact of the virus on the immune system and overall health by further weaking immune functions.[47] Furthermore, recreational drugs can interact adversely with HIV medications, heightening the risk toxicity and impacting the efficacy of ART on HIV disease progression.[48,49] The use of illegal drugs and

alcohol can also undermine adherence to HIV treatment regimens, with individuals often finding it challenging to maintain consistent medication schedules due to impaired focus.[50,51] ART nonadherence allows the virus to proliferate, accelerating the progression from HIV to AIDS and leading to a greater risk of opportunistic infections, cancers, and other life-threatening conditions.[52-54]

Mental health issues, including depression and trauma, play a critical role in ART adherence and viral suppression as its impact can be seen at every step of the HIV Care Continuum.[55] Individuals grappling with these mental health challenges often find it difficult to remain in care and maintain the strict regimen required for effective antiretroviral therapy.[56] Depression, for instance, which symptoms include lack of motivation, forgetfulness, or a sense of hopelessness, may affect an individual's ability to consistently take their medication as prescribed.[57-59] Similarly, trauma or Post Traumatic Stress Disorder (PTSD), especially when unaddressed, can disrupt daily routines and exacerbate feelings of despair or disconnection from one's healthcare needs.[60] These psychological barriers hinder adherence and thus directly impact viral suppression outcomes, as the irregular adherence to ART allows the HIV virus to replicate, increasing the viral load among PLWH.

Research has also established that physiological challenges, such as chronic pain and limitations in performing activities of daily living (ADLs), significantly influence ART adherence and, in turn, viral suppression among PLWH. Chronic pain, often due to comorbidities and co-infections, can influence viral suppression through a range of direct and indirect mechanisms. In studies examining pain severity and adherence to medication such as analgesics, investigators found pain intensity to be negatively correlated with analgesic adherence.[61] Experiences of moderate or severe pain may lead to or intensify symptoms of mental health

issues, such as depression, complicating adherence to complex treatment regimens.[62] Some literature suggests that the relationship between pain and adherence can be explained by cognition issues that are seen among individuals living with severe pain.[63] Patients undergoing treatment for chronic pain frequently report difficulties in cognitive functioning (memory, attention, etc.) impacting their capacity to maintain their ART regimen.[64]

Specific Aims

In this dissertation, we take on a comprehensive investigation aimed at unraveling the intricate dynamics between various factors and their impact on viral suppression among PLWH. With a focus on specific geographic locations, the nuances of individual experiences, and the overarching influence of socio-economic elements, our research is structured around three distinct yet interconnected aims. These aims are meticulously designed to shed light on how neighborhood and community environments, individual health experiences, and self-assessed quality of life influence the health outcomes of individuals navigating the complexities of living with HIV. Below, we outline the specific objectives and hypotheses that guide our exploration:

Aim 1

1) To examine neighborhood factors associated with proportion of PLWH who are virally suppressed in Los Angeles County (CA), San Diego County (CA), and Orange County (CA).

   Hypotheses: (i) Neighborhoods with low walkability and transportation scores will have lower proportions of viral suppression among the population of PLWH;

   (ii) Neighborhoods where residents have a greater average commute time to work will have lower proportions of viral suppression among the population of PLWH.

2) To assess the association between socio-economic factors and proportion of PLWH who are virally suppressed in Los Angeles County (CA), San Diego County (CA), and Orange County (CA).

   Hypotheses: (i) Neighborhoods with a lower median income and a lower proportion of residents with health insurance will have lower proportion of PLWH who are virally suppressed.

   (ii) Neighborhoods with a larger proportion of people with a bachelor's degree or higher will have a higher proportion of PLWH who are virally suppressed.

Aim 2

1) To assess the association between perceived pain and viral suppression among women living with HIV.

   Hypothesis: The odds of viral suppression will be lower among those reporting of moderate/severe pain compared to those reporting no/mild pain.

2) To examine whether substance use modifies the association between participant perceived pain on viral suppression among women living with HIV.

   Hypothesis: The association between pain and viral suppression will vary across different levels of participant reported substance use.

Aim 3

1) To assess the longitudinal association between perceived quality of life and viral suppression status among WLWH in the WIHS cohort.

   Hypothesis: As the quality of life score increases, the odds of viral suppression among WLWH will also increase.

2) To examine whether racial/ethnic minority status modifies the association between perceived quality of life and viral suppression status among WLWH.

   Hypothesis: The association between the perceived quality of life score and viral suppression status will vary across different levels of racial/ethnic minority status. Specifically, we will see greater effect sizes among White WLWH and smaller effect sizes among Black WLWH.

Contributions to Science

This project significantly enhances the scientific understanding of HIV management by addressing critical gaps in the literature through a comprehensive examination of a wide range of factors—including pain perception, quality of life, and socio-environmental influences—and their impact on viral suppression among PLWH. Firstly, by investigating the association between perceived pain and viral suppression, this research sheds light on a relatively underexplored area, highlighting how experiences of pain can influence treatment adherence and HIV health outcomes. Literature examining the association between pain and viral suppression is limited among populations of women living with HIV. The proposed analysis is a beneficial extension of existing studies that have reported on pain frequency prevalence.[65,66]

Secondly, the examination of the relationship between self-perceived quality of life and viral suppression sheds light on the critical role that psychosocial factors play in the effective management of HIV. This approach highlights the necessity of adopting comprehensive care strategies that encompass not only the biomedical aspects of treatment but also address the psychological and social needs of individuals living with HIV, thereby contributing to a more nuanced understanding of patient-centered care. Given that literature highlights differences in HIV treatment rates and health outcomes by race/ethnicity, investigating the modifying role of

racial/ethnic minority status on the association between quality of life and viral suppression is an important key for developing equitable, effective, and personalized healthcare solutions in HIV management. This intersectional approach recognizes that social and behavioral determinants, such as substance use and socioeconomic conditions, often have a differential impact on various racial groups.

Lastly, by leveraging a comprehensive dataset that integrates and harmonizes data from multiple publicly available resources, the project offers a unique exploration of neighborhood and community-level determinants of viral suppression. In addition, given that data from county Departments of Public Health are frequently presented as a proportion, this analysis contributes to a select body of research employing beta regressions to more accurately model these proportionate outcomes.

Chapter II. Study 1: The Intersection of Place and Health: Neighborhood and Socio-Economic Determinants of Viral Suppression.

Abstract

Background: Despite the availability of programs like Ryan White-funded clinics that provide free access to HIV healthcare, significant disparities in viral suppression rates exist. This study investigates whether neighborhood characteristics and sociodemographic factors impede access to these services among people living with HIV (PLWH) in Southern California.

Methods: Data for this study came from the HIV Implementation Science Coordination Initiative, focusing on 40 zip codes in Southern California. Data on viral suppression and neighborhood factors such as walkability, public transit score, and socioeconomic indicators were analyzed using beta regression models to assess what factors are associated with the proportion of PWLH who are virally suppressed per zip code.

Results: Contrary to expectations, higher walkability scores were associated with lower levels of viral suppression. In line with our hypotheses, longer commute times were negatively associated with viral suppression. Employment showed a positive association with viral suppression, while higher poverty levels and longer work hours negatively impacted viral suppression rates. Additionally, no significant relationships were found between education level, public transportation score, and viral suppression.

Conclusion: Results from this study highlight the association between neighborhood characteristics and socioeconomic factors and viral suppression among PLWH in Southern California. The findings emphasize the need for tailored interventions that address specific community needs and barriers to effectively improve HIV treatment outcomes. Future research should incorporate more comprehensive variables and conduct comparative studies across

different geographic regions to improve strategies for enhancing health outcomes in populations affected by HIV.

Keywords: HIV; Viral Suppression; Neighborhood Factors; Socio-Economic Factors

Background

Gaps and Geographic Disparities in Viral Suppression

The HIV epidemic in the U.S. remains a significant public health challenge. At the end of 2020, approximately 1.2 million people in the U.S. were living with HIV, with an estimated 34,800 new diagnoses reported that year. With the development of ART, which has shown to improve health outcomes and reduce transmission risk, recent interventions focus on barriers to accessing care to achieve and maintain viral suppression.[67]

While much progress has been made in addressing challenges to accessing HIV treatment, many hurdles remain before reaching the goal of the Ending the HIV Epidemic (EHE) Initiative of reducing new HIV infections by 75% and increasing the percentage of PLWH who are virally suppressed to 95% by 2025.[68,69] Despite the critical support provided by government-funded programs, disparities in health outcomes, particularly viral suppression rates, persist across different regions. Currently only 66% of PLWH in the U.S. are virally suppressed, with some regions reaching levels as low as 14% and others as high as 93%.[70,71] This inconsistency underscores the importance of examining a broader spectrum of factors impacting access to treatment. Investigating social determinants of health, including socioeconomic status, as well as examining barriers to engagement with healthcare services, such as ease of access to medical facilities is essential. The challenge of gathering diverse data sets, coupled with the need for employing specific types of data analysis techniques to effectively analyze and interpret data from publicly available sources, poses a significant barrier in understanding the factors influencing HIV treatment needs, identifying which geographies are most impacted, and developing targeted, effective interventions.

Comprehensive Datasets & Identifying Barriers to Care

By analyzing integrated datasets, we gain valuable insights into specific factors within communities that are closely linked to HIV treatment outcomes. Although few studies utilize integrated public datasets, many have used public datasets such as AIDSVU and the US Census as part of their research studies.[31,72,73] Rosenberg et al. assessed HIV prevalence and incidence rates among men who have sex with men (MSM) at the national, state, and county level to provide updated local estimates using the AIDSVU database.[73] Rossheim et al. sourced data from the U.S. Census Bureau to examine the association between on- and off-premise alcohol retail outlets and HIV prevalence across 1,523 counties in the U.S.[74] Results from these studies can help prioritize communities based on their level of need, thereby identifying key areas and populations where interventions can be targeted effectively.

Large datasets have proven invaluable in investigating risk factors, generating hypotheses, and exploring avenues for HIV interventions.[75-77] However, most are focused on specific areas and themes, with only a handful encompassing multiple topic domains. The integration and combination of datasets across different geographic areas holds significant potential for enhancing our comprehension of social and structural determinants of health, barriers to care, and the HIV care continuum. A recent example of data integration is the HIV Implementation Science Coordination Initiative (ISCI; protocol 001) study, "Identifying Optimal Rapid START Implementation Strategies to End the HIV Epidemic in the U.S." whose goal is to inform strategies to scale-up implementation of rapid status neutral antiretroviral therapy (rapid START) within and across EHE priority areas. The integrated datasets permit a more comprehensive exploration of factors which may impact viral suppression. For instance,

neighborhood characteristics as well as socio-economic variables may play a role in preventing people from accessing HIV treatment services.

Social Determinants of Health & Viral Suppression Disparities

The impact of public transportation and neighborhood walkability on HIV health outcomes, particularly in the context of accessing healthcare services, is significant and multifaceted. Efficient transportation systems and walkable neighborhoods facilitate easier access to healthcare facilities, pharmacies, and health-related services, reducing barriers to care that many individuals face, especially those in under-resourced or rural areas. In a qualitative study of barriers to retention in care among women living with HIV in the U.S., transportation was identified as a primary obstacle to attending clinic appointments.[78] Similar results were seen in a study among pregnant woman where 20% of participants reported transportation as a barrier to accessing substance use treatment facilities.[79] Access to public transportation or walkable neighborhoods, which minimizes the dependence on private vehicles, may reduce transportation-related barriers to accessing HIV treatment services.

Similarly, an individual's average daily time commuting to and from work may impact health outcomes through a variety of pathways. In a 2019 study examining how commuting affects wellbeing, results demonstrated that an increase in commute time was associated with poorer mental health and greater strain.[80] In a similar study examining differences in this association by sex, longer duration commutes were found to negatively impact mental health in women, but not in men.[81] These findings are valuable for researchers investigating obstacles to accessing HIV treatment, given the direct correlation between poor mental health and an individual's adherence to medication regimens and engagement in care.[55,82]

Socioeconomic factors also play a pivotal role in influencing health outcomes for individuals living with HIV, particularly in the context of achieving and maintaining viral suppression.[83] Employment status, health insurance coverage, and educational attainment are among key determinants that can significantly impact an individual's ability to access and adhere to ART.[84] Employment provides not only financial stability but also entry to employer-sponsored health insurance programs, which can facilitate easier access to healthcare services and ART medications.[85] Conversely, unemployment or underemployment may lead to lapses in health insurance coverage, presenting substantial barriers to consistent HIV care.[86] In a study examining the impact of social determinants on ART access and HIV outcomes among 8,000 individuals living with HIV, those without employment or with unstable jobs, along with those having lower levels of education, demonstrated a lower 1-year probability of achieving viral suppression.[87] Similarly, a systematic review of 28 published articles highlighted the positive association between employment and adherence to ART in high income areas.[88]

Literature also emphasizes how education level correlates with health literacy, which affects an individual's understanding of their health condition, engagement in care, and ability to navigate the healthcare system effectively. When examining structural determinants of ART use in a geographically diverse sample of PLWH, researchers noted that those residing in areas characterized by greater disadvantage (as determined by a composite score based on Census indicators, such as the percentage of individuals without a high school diploma) were found to be less likely to report ongoing use of ART.[83]

Furthermore, health insurance stands out as an important element in achieving viral suppression among individuals living with HIV. Insurance increases access to ART as well as a wide array of healthcare services, such as consistent viral load monitoring, immune function

assessment, and support mechanisms that assist in adhering to medication regimens (counseling services, case management, etc.). When examining areas for early intervention among high-risk populations, researchers found that lack of health insurance, especially among those living with HIV, obstructed the receipt of primary care services.[89] On a similar note, when investigating the effect of health insurance on the likelihood of HIV transmission among those treated with ART, individuals with insurance were found to have over 50% reduced odds of exhibiting an HIV viral load exceeding 1500 copies/ml (OR: 0.46; CI: 0.26–0.84).[90]

These socioeconomic factors intersect to create a complex web of challenges and facilitators that influence viral suppression rates among PLWH. Understanding these dynamics is crucial for designing interventions that address the broader determinants of health and improve viral suppression outcomes.

Existing Initiatives for Overcoming HIV Care Challenges

Introduced in 1990, the Ryan White HIV/AIDS Program was created as response to the critical need for care and treatment services for individuals living with HIV/AIDS in the United States, particularly those with limited or no access to adequate healthcare.[91] The introduction of the program and its funded clinics aims to bridge the gap in healthcare access and ensure that those living with HIV can receive the comprehensive treatment and support services necessary. Ryan White-funded clinics are healthcare facilities that receive support from the Ryan White HIV/AIDS Program and play a crucial role in the public health system by offering a comprehensive range of services tailored to the needs of PLWH.[92] Services provided include primary medical care, medication, case management, and support services aimed at enhancing the quality of life for patients.[92,93]

While numerous studies have explored the impact of HIV prevention and treatment

services offered by Ryan White-funded clinics, they predominantly analyze the clinics' direct impact or examine overall facilitators and barriers to treatment within specific geographic regions or cities.[93-96] The present study shifts the focus from the clinics to the neighborhoods surrounding these clinics, exploring why disparities in viral suppression rates persist despite the availability of free HIV treatment services at these clinics across the U.S. By analyzing neighborhood characteristics, this research aims to uncover potential barriers, such as transportation issues, that may hinder individuals from seeking treatment. This approach will enable a deeper understanding of the environmental and social determinants affecting viral suppression rates among communities served by Ryan White clinics. Additionally, recognizing that most publicly available datasets report HIV outcomes as proportions, which poses analytical challenges, this study employs an underutilized statistical method that allows for the analysis of such variables.

The goal of this study is to use a subset of the integrated dataset from ISCI protocol 001 to examine how transportation related neighborhood characteristics and socio-economic factors are associated with viral suppression in Southern California neighborhoods.

Methods

Dataset

This research undertakes a comprehensive analysis by integrating and linking multiple publicly available datasets, including national, state, and clinic-level data, across priority jurisdictions of the EHE initiative. To maximize its effectiveness, the EHE targets its initial efforts towards 48 counties —areas that account for over half of the HIV diagnoses in the U.S.[69] While various studies have focused on specific themes or areas that impact HIV treatment services, few cover multiple topic domains. This integrated dataset allows for the exploration of

how social and structural determinants of health vary across geographies and which indicators are predictive of adherence to HIV treatment. Identifying these factors will aid in developing evidence-based interventions for improved health outcomes for PLWH.

As part of ISCI protocol 001, a collection of publicly available datasets was created to facilitate a holistic analysis of HIV-related care in support of EHE goals across the Ryan White-funded clinics in the U.S. The building of the database occurred over three primary phases: initial sourcing of ideas and metrics, reviewing and building the database, and then final quality controls and verification. Variables from the linked datasets were tagged to the 108 Ryan-White associated clinics of interest across various levels of geography: state, county, zip code. States covered by the clinics of interest include Alabama, California, Illinois, Maryland, and Texas. Where possible, the most recent data available was sourced (2021-2022 data).

The proposed study will use a subset of the primary dataset, focusing on Southern California counties: Los Angeles, Orange, and San Diego. For this analysis, we selected zip codes which had data on the proportions of people who were virally suppressed (n= 40). Consequently, zip codes without such data were excluded. Information was sourced from the following publicly accessible sources:

1) US Census 2020 (data.census.gov)
2) AIDSVU (aidsvu.org)
3) Walk Score (Walkingscore.com)
4) The Center for Neighborhood Technology (CNT; alltransit.cnt.org)
5) Los Angeles Department of Public Health (http://publichealth.lacounty.gov)
6) San Diego County Public Health Services (Sandiegocounty.gov/hhsa/programs/phs/)

Measures

Dependent Variable:

Viral Suppression – The primary outcome of interest in this study is the proportion of PLWH who are virally suppressed at the zip code level. Data was sourced from AIDSVU and the Los Angeles County and San Diego County Departments of Public Health.

Independent Variables:

Neighborhood variables include:

- Walkability – The neighborhood walkability variable measures walkability by zip code on a scale from 0 - 100 based on walking routes to destinations such as grocery stores, schools, parks, restaurants, and retail. Walkability data was sourced from walkingscore.com.
- Public transit score – The Transit Performance Score measures more than just access to transit. It considers the performance of transit - connections to other routes, jobs accessible in a 30-minute transit ride, and the number of workers using transit to travel. All neighborhoods in cities with over 100,000 population are ranked and given a score from 1 to 10. Data was sourced from The Center for Neighborhood Technology (CNT; alltransit.cnt.org)
- Commute time – The commute variable measures mean travel time it takes for individuals to commute from their home to work in minutes. Commute time data was sourced from the US Census Bureau.
- Health People Index (HPI) – The HPI is an index score that includes 25 community characteristics, such as housing, education, and more which is often used to describe

community conditions associated with life expectancy. The scores range from 0 – 100, where a higher HPI score indicates a healthier community.

Socioeconomic variables include:

- Employment – Percent of population living within a zip code identified as working a job, either full time or part time. Data on employment was sourced from the US Census Bureau.
- Education – Percent of population within a zip code with a bachelor's degree or higher. Data on education was sourced from the US Census Bureau.
- Poverty – Percent of population within a zip code who are considered to be living in poverty by the U.S. Census guidelines and calculations. The Census Bureau uses a series of income thresholds based on family size to identify people and families who falls below the poverty line. If the total income of an individual or a family fall below the threshold, then that family and all its members are classified as being in poverty.
- Work Hours – Average amount of hours worked per week within a zip code.

Additional covariates include:

- Health Insurance – Percent of population under the age of 65 years living within a zip code identified as not having health insurance. Data on health insurance status was sourced from the US Census Bureau.
- Family Size – Average household family size within a zip code.

Selection of the covariates is based on prior knowledge, literature, and directed acyclic graphs (DAG) for the relationship between viral suppression and the neighborhood factors as well as socio-economic factors available in the dataset. The simplified and time-varying DAG is seen in Figure 4.1 and 4.2.

Data Analysis

The distribution of the variables of interest were assessed to identify influential observations/outliers, skewness, and missing data. We examined the crude and adjusted associations between neighborhood-level factors and socio-economic factors with proportion of PLWH who are virally suppressed in the zip code using beta regression models. Given that the outcome of interest is a proportion with values that fall between zero and one, using traditional regression models, such a linear regression, are not advised since results may include fitted values for the variable of interest that exceed its lower and upper bounds.[97] Although transformation of the dependent variable is a potential solution, interpreting the model's parameters in relation to the initial response variable becomes challenging.[98] Additionally, proportional data often exhibits skewness, making conclusions drawn from the presumption of normal distribution potentially inaccurate.[99]

Thus, beta regression is introduced as an appropriate method for analyzing data where the dependent variable is measured continuously on a standard unit interval, as in this study. By using this method, we are assuming that the dependent variable follows a beta distribution.[97,98] One should note that a beta distribution excludes the values zero and one, however, the dependent variable of the proposed study only includes values greater than zero and less than one. All data management, processing, descriptive analyses, and statistical modeling were done using STATA 16,[100] and interpretation of statistical significance is guided by confidence intervals.

Results

The ISCI protocol 001 dataset includes 104 Ryan-White clinics that fall within 79 unique zip codes, 15 counties, and 5 states. Table S1 presents zip code, county, and state-level

characteristics of the primary national dataset. At the national level, 66% of PLWH are virally suppressed. Across the fifteen counties included in the overall dataset, the mean percent of PLWH who are virally suppressed is 61%.

As previously mentioned, the current study utilizes a subset of 40 zip codes from the primary dataset focused on the Southern California region. Table 2.1 presents the distribution of the covariates. The mean percentage (SD) of PLWH who are virally suppressed is 62.5% (7.4%), with neighborhood variability ranging from 43% to 75%. The mean walkability score among all 40 zip codes was 71, with some areas scoring as low at 16 and others as high as 95. The mean public transportation score was 8 and the mean HPI score was 37.7. The HPI score also had great variability among neighborhoods where values ranged from 4 – 91.

Median household income shows substantial variability, with an average of $65,574 and a range from $24,853 to $123,955, indicating a wide economic disparity between the highest and lowest income zip codes. Employment rates average at 61%, with a standard deviation of 10.0, reflecting a moderate level of employment across regions. Educational attainment, reported as the proportion of individuals within the zip code with a bachelor's degree or higher, also varies significantly, from 6.4% to 70.8%, averaging at 34.3%.

The demographic data further reveal that an average of 16.4% of the population lives in poverty, with the percentage ranging from 7.4% to 45.8%, highlighting considerable socioeconomic disparities and mirroring what was seen among median household incomes. The average family size is relatively stable across zip codes, with an average of 3.4 members per family.

Association Between Viral Suppression and Neighborhood Factors

The beta regressions identified negative associations in our study, showing that both higher walkability scores (coefficient = -0.003, [-0.006, -0.0002]) and longer average commute times to work (coefficient = -0.021, [-0.04, -0.0001]) are linked to lower levels of viral suppression among PLWH. In contrast, the public transportation score (coefficient = -0.039) and the Healthy People Index (coefficient = 0.004) did not demonstrate a clear association with viral suppression proportions, suggesting that these factors may not be significantly associated in our study sample.

Association Between Viral Suppression and Demographic/Socioeconomic Factors

The percentage of employed individuals revealed a positive association with viral suppression (coefficient = 1.41, [0.33, 2.48]), indicating that higher employment proportions correspond to higher proportions of individuals who are virally suppressed within each zip code. Conversely, the average work hours per week showed a negative association (coefficient = -0.053, [-0.102, -0.004]), where longer work hours correlated with lower proportion of viral suppression. We also found a strong negative association for the percent of people who are living in poverty (coefficient = -4.25, [-5.78, -2.75]), showing that zip codes with higher poverty levels are significantly associated with lower proportions of viral suppression among PLWH. When examining education, we did not observe an association between proportion of PLWH who are virally suppressed and precent of population who report obtaining a bachelor's degree or higher (coefficient = -0.376, [-0.845, 0.092]).

Discussion

This study provides a detailed examination of the association between neighborhood characteristics, socioeconomic factors, and viral suppression among PLWH in Southern

California, particularly in areas with Ryan White clinics offering free HIV healthcare services. One of the more unexpected results was the negative association between walkability scores and viral suppression. We hypothesized that greater access to walkable environments, particularly for individuals with limited transportation options, might facilitate easier access to clinics, potentially improving health outcomes for PLWH. However, several non-examined factors could explain the contrary results we saw in our analysis. One possible reason is the planning and design of Southern California neighborhood as well as unmeasured confounding effect of neighborhood violence and safety. Many high-income and low violence neighborhoods in Southern California, such as Malibu and La Jolla, have low walkability and public transportation scores. This is likely due to economic segregation and a history of urban zoning laws and planning strategies that were racially and economically exclusionary, making it so that people from a lower socioeconomic status do not have access to public resources and spaces in these affluent communities.[101,102] Conversely, there are neighborhoods with disproportionately higher violence or crime rates that are highly walkable. Higher violence rates in a neighborhood could discourage residents, particularly those with compromised health, from utilizing nearby healthcare facilities, including Ryan White funded clinics.

The association between longer average commute times and lower viral suppression underscores how daily travel can complicate health management for PLWH. Extended commutes not only may increase stress but also reduce the time available for healthcare visits, particularly impacting those who work regular business hours. Similarly, our analysis revealed a negative association between average number of hours worked per week and viral suppression, where longer work hours were associated with a lower proportion of viral suppression. Both extended commutes and increased work hours can lead to scheduling conflicts, often meaning that by the

time these individuals are available, clinics may have already closed. This impedes consistent access to necessary care and treatment adherence, which are crucial for maintaining viral suppression. These findings highlight the need for workplace policies that support the healthcare needs of employees, particularly those managing chronic conditions like HIV, to improve health outcomes and facilitate sustained viral suppression.

Results from the study also indicated no significant association between the HPI score and viral suppression, suggesting that the HPI may not capture all relevant health factors specific to PLWH. This outcome might reflect limitations in the HPI's ability to account for the nuanced needs and challenges faced by this population, especially in terms of healthcare access and quality. The analysis also revealed no association between the public transportation score and viral suppression. This suggests that while research shows that these factors are integral to general urban planning and public health strategies, they may not sufficiently address the unique barriers faced by this population, such as clinic hours aligning with work schedules or specific healthcare needs. Or in the case of our study, it might not be as impactful in the Southern California region. Further research could explore how and in what populations these elements might be tailored to better support viral suppression among PLWH.

On the demographic and socioeconomic front, the positive correlation between employment rates and viral suppression underscores the potential benefits of economic stability in managing HIV. Employment might improve access to health insurance, healthcare services, and support systems, facilitating better health outcomes. Conversely, the strong negative correlation between poverty levels and viral suppression emphasizes the detrimental impact of socioeconomic hardship on health outcomes. High poverty levels likely reflect broader barriers to healthcare access, including financial constraints that would impact an individuals' ability to

prioritize healthcare over work and family commitments, as well as the limited availability of quality medical care.

Furthermore, the lack of association between educational attainment and viral suppression contradicts some previous studies suggesting that higher education correlates with better health literacy and outcomes.[103] This discrepancy may be attributed to the overriding influence of other socio-economic factors like poverty and employment status within our study population, which could dilute the impact of education alone.

Strengths

This study possesses several notable strengths that improve the relevance and applicability of its findings. First, the inclusion of a comprehensive dataset from various Southern California neighborhoods provides a diverse sample, ensuring a wide representation of different demographic and socioeconomic groups specific to this region. The wide distribution of relevant variables can be seen in Table 2.1. Additionally, while many public datasets measure and report variables as proportions and percentages, beta regression remains an underutilized statistical method. By using beta regression in this analysis, this study not only harnesses the full potential of the data available at various county health departments, but also contributes to the limited number of studies using this technique, potentially encouraging further utilization of this method.

Another significant strength of this study is the successful integration and linkage of datasets from various sources, despite the challenges posed by differing data formats and structures. Considerable efforts in data transformation and harmonization were undertaken to ensure compatibility for analysis. This meticulous process allows for an accurate and

comprehensive evaluation of varying factors that may influence viral suppression among PLWH in neighborhoods with Ryan White clinics.

Limitations

As with most public datasets, the integrated dataset used in this study may vary in terms of data quality and accuracy. Variations or inaccuracies within the dataset can impact the research findings, potentially introducing errors or biases into the analytical process, leading to incorrect conclusions. Additionally, given the necessity to utilize beta regressions due to our outcome being expressed as a proportion, it was not possible to determine the magnitude of the associations observed. This limited our analysis to identifying only the significance and direction of associations.

This study's generalizability is limited due to its focus on a subset of zip codes in Southern California. While the chosen zip codes likely share some characteristics with a broader urban population, they may not represent the full spectrum of socioeconomic conditions, neighborhood environments, or variations in state laws across the country. The associations between neighborhood factors and viral suppression could vary significantly in other geographic regions or in rural settings.

An additional limitation is the potential for unmeasured confounding. Variables not included in our analysis could significantly impact the association observed between our independent and dependent variables. This limitation restricts our ability to draw definitive conclusions from the data. Lastly, the cross-sectional nature of this study prevents us from inferring causality or examining trends over time. This type of study design can only provide a snapshot, limiting our understanding of how associations may evolve or be influenced by changing conditions.

Conclusion

In conclusion, the research question examined in this study is crucial for identifying the disconnect between the presence of healthcare resources and actual service utilization. By examining neighborhood and socioeconomic factors within these areas, the study sheds light on potential obstacles that prevent optimal use of HIV healthcare, thereby informing strategies to enhance access and engagement in treatment. Future research should aim to include more comprehensive variables, such as neighborhood violence, crime rates, or quality of healthcare facilities to better delineate the mechanisms through which neighborhood environments influence health outcomes in this population. In addition, implementing comparative studies across different states or regions could help identify unique challenges and effective strategies tailored to local contexts, enhancing the generalizability and applicability of the findings to broader populations. Interventions aimed at improving viral suppression among PLWH should not only focus on individual behaviors but also consider broader structural changes that improve access to care and reduce socioeconomic disparities, thereby contributing to better public health outcomes.

Tables

Table 2.1. Neighborhood and Demographic Characteristics by Zip Code* (n=40)

Characteristics	Mean	Standard Deviation	Median	Min	Max
HIV Factors					
% Virally Suppressed	62.5	7.4	62.2	43.6	74.7
Neighborhood Factors					
Walkability (0-100)	71.2	20.2	77	16	95
Public Transportation Score (0-10)	8.0	1.4	8.6	4.7	9.8
Mean Commute to Work (Mins)	30.2	4.0	30.7	21.9	37.3
Healthy People Index	37.7	29.7	23.05	3.8	91.4
Demographics& Socioeconomic Factors					
Median Household Income	65,574	22,924	63,634	24,853	123,955
% Employed	61.0	10.0	61.0	43.9	73.6
% With a Bachelor's Degree or Higher	34.3	20.4	33.8	6.4	70.8
% Disabled	11.0	3.9	10.6	6.3	32.7
% Population <65 Years Uninsured	10.1	5.5	9.6	2.3	25.8
Average Work Hours (Per Week)	38.5	1.8	37.8	36.4	44.5
% Living in Poverty	16.4	8.1	13.9	7.4	45.8
Average Family Size	3.4	0.6	3.4	2.3	4.6

*Zip codes utilized in the table are from Los Angeles, Orange, and San Diego County

Table 2.2. Results from the beta regressions[§] examining the association between percent of PWLH who are virally suppressed and neighborhood and socioeconomic variables.

Characteristics	Coeff	Standard Error[*]	P-value	(95% CI)
Neighborhood Factors				
Walkability (0-100)	-0.003	0.001	0.03	(-0.006, -0.0002)
Public Transportation Score (0-10)	-0.039	0.029	0.17	(-0.097, 0.017)
Mean Commute to Work (Mins)	-0.021	0.011	0.04	(-0.04, -0.0001)
Healthy People Index	0.004	0.002	0.08	(-0.0007, 0.01)
Demographics& Socioeconomic Factors				
% Employed	1.41	0.550	0.01	(0.331, 2.487)
% With a Bachelor's Degree or Higher	-0.376	0.239	0.11	(-0.845, 0.092)
Average Work Hours (Per Week)	-0.053	0.024	0.03	(-0.102, -0.004)
% Living in Poverty	-4.25	0 .766	<0.000	(-5.788, -2.755)

[*]Robust standard error was used in the model. [§]Separate models were run for each characteristic, adjusting for appropriate confounding variables such as health insurance status, disability, employment, education, poverty, health insurance, and race.

Chapter III. Study 2: Pain, Viral Suppression, and the Moderating Effect of Substance Use Among HIV-Positive Women in the Women's Interagency HIV Study (WIHS).

Abstract

Background: Living with pain has been shown to impact daily activities, such as medication adherence, which is crucial for managing chronic conditions like HIV. Given that people living with HIV (PLWH) often report higher instances of pain and substance use compared to the general population, the association between pain, substance use, and viral suppression has not been extensively studied among diverse populations of women living with HIV (WLWH). Knowing the critical role of antiretroviral therapy (ART) adherence in achieving and maintaining viral suppression, this study aims to explore how pain and substance use influence this association.

Methods: This study analyzes data from participants enrolled in the Women's Interagency HIV Study (WIHS) across all recruitment sites in 2016. To investigate the association between participant-reported pain and viral suppression, we employed both unadjusted and adjusted logistic regression models. To examine how substance use may modify the relationship between pain and viral suppression, interaction terms for various substances were included in the regression models.

Results: We found that there was no substantial association between pain and viral suppression among WLWH in our cohort. Furthermore, we saw no modification in the association by any type of substance use.

Conclusion: Contrary to what we have seen in previous research, no significant association was found between pain and viral suppression levels in our cohort. This finding may suggest that the

need to maintain close to perfect ART adherence among WLWH in order to ensure proper immune functioning might buffer against the negative impacts of pain on medication adherence.

Keywords: Pain; Viral Suppression; Substance use; HIV

Background

HIV in the Age of ART

The development and expansion of antiretroviral therapy (ART) revolutionized the landscape of HIV treatment and care, offering numerous benefits to PLWH. Adherence to ART reduces the HIV viral load in PLWH, allowing them to achieve viral suppression, defined as having less than 200 copies of HIV/ml of blood.[104] Viral suppression essentially eliminates the risk of HIV transmission to sexual partners, as well as significantly reduces AIDS-related illnesses and opportunistic infections.[28] ART is also responsible for enhancing immune function, resulting in prolonged life expectancy and improved overall health among PLWH.[105,106] Despite these benefits, many intrapersonal and psychosocial factors are shown to influence ART adherence. For example, the psychological stressors of living with a chronic illness, coupled with the stigma surrounding HIV can contribute to elevated rates of depression, anxiety, and PTSD, all of which are highly associated with poor engagement in HIV related care and suboptimal ART adherence.[107-109] PLWH also have higher rates of substance use compared to the general population.[110] Some individuals may turn to substance use as a coping mechanism for the unique stressors associated with HIV, which can further complicate health management and adherence.[111] PLWH also report higher prevalence rates of pain compared to the general population, potentially impacting activities of daily living such as adhering to medication regimens. [112]

Pain, ART adherence and Viral Suppression

The association between pain and viral suppression is an important area of investigation due to the impact of moderate to severe pain on activities of daily living such as medication adherence.[113,114] Experiences of pain, often attributed to HIV-related neuropathy or

musculoskeletal conditions, have been consistently linked to suboptimal adherence to ART regimens.[44,115,116] One critical aspect of this association is the psychological and emotional toll that pain takes on PLWH. Long-term experiences of pain can lead to depression, anxiety, and overall reduced quality of life, making the daily regimen of medication management even more challenging.[117-119] The experience of pain itself can become a powerful distraction and source of distress, diverting attention away from medication adherence.[120] Moreover, pain can directly influence medication-taking behavior through a variety of pathways. Individuals with pain may perceive their antiretroviral medications as exacerbating their discomfort, leading them to skip doses or modify their dosing schedules without medical guidance.[121,122] The fear of side effects interacting with existing pain symptoms can also lead to non-adherence, as patients attempt to manage their symptoms independently.[123]

Variation in Pain by Sex

While PLWH face a higher burden of pain compared to their seronegative counterparts, research has identified differences in experiencing and treating pain between sexes. Findings from Centers for Disease Control and Prevention (CDC) report higher rates of chronic pain and high-intensity chronic pain among females compared to males.[124] When examining population-level prevalence rates, common pain-related illnesses such as fibromyalgia and migraines are more common among women, possibly due to differences in hormones and neural pathways, higher rates of depression, as well as social factors such as post-traumatic stress disorder.[125-128] The risk for migraines is greater among individuals with post-traumatic stress disorder, which is seen more often among females due to their higher rates of intimate partner violence and sexual assault.[129,130] Similarly, depression which is more commonly diagnosed in women increases the risk of migraines by two-fold.[131] Females are also less likely to receive treatment for pain

compared to their male counterparts despite reporting experiences of pain more often.[132,133] Part of this can be attributed to sex and gender biases in how medical providers assess pain in females compared to males. Recent studies have highlighted the existence of incorrect assumptions that women have a heightened sensitivity to pain and are prone to overstate or dramatize their discomfort which may lead to undervaluing both the verbal and non-verbal indicators of pain presented by female patients.[132,134] Research on pain and analgesic treatment demonstrates that women are less likely to receive pain medication and analgesics for the same medical ailments than their male counterparts, and on average wait longer to receive pain medication in inpatient and outpatient medical settings, even after adjusting for pain score.[135,136]

Substance Use as a Potential Modifier

While examining the relationship between pain, medication adherence, and viral suppression among PLWH, substance use can potentially serve as a modifier in the pain-viral suppression relationship.[137] Research has continuously demonstrated that substance use is higher among PLWH than the general population and numerous studies have identified substance use as a common barrier to ART adherence and viral suppression.[138] From a biological prescriptive, the drug-drug interaction between ART and substances has been shown to impact the toxicity and efficacy of ART through metabolic pathways.[48,139,140] Methamphetamine impacts ART efficacy through its interaction with metabolic enzymes like CYP2D6 and CYP3A4, leading to altered metabolism of antiretrovirals and potentially increased toxicity.[48,141] Cocaine and opioids affect ART by influencing the activity of CYP3A enzymes, which can result in reduced drug efficacy due to altered antiretroviral metabolism and increased risk of ART toxicity.[49]

Substance use not only influences the coping mechanisms and health behaviors of these individuals but could further complicate the association between pain and viral suppression by

impacting their engagement in activities of daily living, including health practices such as medication adherence.[50] Substance use has the capacity to exacerbate the challenges faced by individuals in managing their health regimen. For instance, substance use can impair cognitive functions and decision-making abilities, leading to decreased medication adherence.[51,142] This impairment can be particularly detrimental in the context of managing HIV, where strict adherence to ART is essential for achieving and maintaining viral suppression.[29]

Examining the relationship between pain and viral suppression, as well as the potentially moderating role of substance use in the pain-viral suppression association allows researchers to determine effective areas of intervening, either in the form of treatment interventions to manage pain or in the form of substance use treatment programs. This integrated approach is key to mitigating the negative impact of pain on medication adherence and enhancing health outcomes for PLWH, especially in populations using legal and illegal substances.

Methods

Study Sample & Design

The Women's Interagency HIV Study (WIHS) is a comprehensive cohort study that has been examining women living with HIV (WLWH) across the United States since 1993.[143] Initially, the cohort included six sites located in Brooklyn, NY; the Bronx/Manhattan, NY; Washington, DC; Chicago, IL; San Francisco, CA; and Los Angeles, CA. In 2013, four additional sites in the southern United States were added: Chapel Hill, NC; Atlanta, GA; Birmingham, AL/Jackson, MS; and Miami, FL.[144] The WIHS cohort consists of 4,982 women enrolled across four waves between 1993 and 2015. At baseline, 3,677 women were HIV-seropositive, and 1,305 were HIV-seronegative, with 26 of the latter group seroconverting during the study period.[145] Eligibility for HIV-positive women required documented reactive HIV

serology and confirmatory tests, with the inclusion of those on highly active antiretroviral therapy (HAART) as per US consensus treatment recommendations.[145]

As of October 2016, the WIHS cohort is actively following 2,363 women. Since its inception, the cohort has seen 1,268 deaths, 130 withdrawals, and losses due to administrative reasons or lost to follow-up, highlighting the challenges and complexities of managing a long-term observational study in a diverse and dynamic population.[145]

The majority of the study's participants live below the poverty line, with 64% of those who are HIV-positive and 56% of those who are HIV-negative reporting annual household incomes of $18,000 or less. Educational attainment is low among the cohort, with about one-third of both HIV-positive and HIV-negative participants having not completed high school. Nearly all WLWH (97%) have accessed ART at some point, and 89% were on ART at their most recent study visit. However, despite widespread ART use, 31% of these WLWH still exhibit unsuppressed HIV viral loads, indicating ongoing challenges in achieving optimal outcomes in HIV care.[145]

The current study will utilize data from participants enrolled in the WIHS study in 2016 across all sites. The visit number associated with this year is 44. As part of the study visit, information on medical history substance use, sexual behavior, health care utilization, and psychosocial and behavioral factors are collected. In addition to data collected via interviews, participant blood, urine, and cervicovaginal swabs are also collected for testing.

Variables

Dependent Variable:

Our primary outcome is viral suppression. Viral load <200 copies/ml will be identified as

virally suppressed and viral load >200 copies/ml will be labeled as not virally suppressed. Viral load is measured using the Abbot m2000 HIV-1 RealTime System at the time of each study visit.

Independent Variables:

Participant-reported pain is the primary predictor of interest. Pain is measured using a single-item tool measuring amount of bodily pain over the four weeks prior to the participant visit. Response options include “No Pain”, “Very Mild”, “Mild”, “Moderate”, “Severe”, and “Very Severe”. Responses were dichotomized into a No/Mild Pain category and a Moderate/Severe Pain category.

The potential moderating variables are related to substance use. Substance use is measured in the WIHS cohort by asking participants to respond “Yes” or “No” if they have used the following substances since their last study visit: cocaine, heroin, illicit methadone, amphetamines, injection drugs, non-injected recreational drugs (hallucinogens), methamphetamines. Marijuana use (“Yes” vs “No”) was defined as using marijuana since last study visit and heavy alcohol consumption (“Yes” vs “No”) was defined per CDC guidelines for women.[146] To ensure sufficient sample sizes, substance use was categorized into the following categories: heavy alcohol use, cannabis use, stimulant use, and use of other substances.

Covariates/Confounders:

Covariates include depression (defined as having scores ≥16 using the Center for Epidemiologic Studies Depression (CES-D) scale),[147] employment status (Employed, Unemployed, or Unknown), health insurance (Insured or Uninsured), years living with HIV (number of years since participant first tested seropositive for HIV), race/ethnicity (Hispanic, Non-Hispanic white, Non-Hispanic Black, Other/Unknown), sexual orientation (Heterosexual, Gay, Bisexual, Other), age at visit (years), highest education level at time of visit (options

include: Below high school (HS), Some HS diploma/Equivalent, Some/Completed higher education), current cigarette smoking status (Not Smoking or Smoking), cancer diagnosis (Yes if participant reports having a history of cancer diagnosis), hospitalization ("Yes" if participant report hospitalization since their last visit), pain medication use ("Yes if participant reports using for NSAIDS, Steroidal Anti-Inflammatories, Antidepressant, Anticonvulsant/Antiepileptic drugs, Topical Anesthetics, Mild Opioids, Sleeping medication, muscle relaxant, anxiety medication, or migraine medication for pain), and any STI diagnosis ("Yes" if participant tested positive for Gonorrhea, Syphilis, Chlamydia, PID, Genital Herpes, Genital Warts, Trichomonal Vaginitis, Bacterial Vaginitis). A polysubstance use variable was also created to capture participants who report using more than two substances since their last visit.

Selection of the covariates is based on prior knowledge and literature, as well as directed acyclic graph (DAG) for the relationship between pain and ART adherence as seen in Figure 3.1. Frequency of missing data per variable can be seen in Figure S1.

Inclusion/Exclusion Criteria

The study population consists of HIV seropositive women who were under observation in the WIHS cohort. Serostatus is verified using documentation of a reactive HIV blood serum and confirmatory test, reported having been prescribed antiretroviral therapy at any study visit, and who provided information on substance use since their last study visit.

Data Analysis

Analyses were performed using STATA 16.[100] Interpretation of statistical significance was guided by confidence intervals. The distribution of the variables of interest were assessed to identify influential observations/outliers, skewness, and missing data. Means (SD) and frequencies (percentage) are provided to describe the sociodemographic characteristics of the

patients at the time of visit. The variables described above were compared by pain status using Pearson's chi-square tests for categorical variables and two-sample t-tests for continuous variables. We use unadjusted and adjusted logistic regression models to assess the association between participant pain and viral suppression, while controlling for potential confounding variables. Three models will be presented, demonstrating the estimates as various confounders are added to the model. Model A includes the study exposure, demographic characteristics, and variables related to socioeconomic status. Model B includes all variables from Model A as well as variables related to participant health status and use of any medications to address pain. Lastly, the fully adjusted model (C) has additional variables regarding substance use. To examine substance use disparities in this association, we will include an interaction term in the model.

Results

Demographic and Socioeconomic Characteristics

The average age of the overall cohort is 49 years (SD = 9, range [26 – 81]). Approximately, 90% are heterosexual; 14% are Hispanic and 73% Black/African-American. More than 97% report health insurance coverage, and 75% make an income below 200% of the federal poverty limit (less than $2,000 per month). Sixty-five percent are unemployed, and there are roughly an equal number of participants with below a high school education, a high school education or equivalent degree, and those with an advanced degree (33.7%, 30.7%, 35.6%, respectively).

Health Behaviors

Forty percent of the cohort are current cigarette smokers, 19% have smoked marijuana since their last visit, and almost 11% report heavy alcohol consumption as defined by the

CDC.[146] Six percent report stimulant use, 2.4% report using other substances such as opioids, tranquilizers, and hallucinogens, and 2.4% report using more than three illegal substances.

Health Status

Thirty percent of the cohort meets the diagnostic criteria for depression and 35% report having moderate to severe pain in the last four weeks, 25% report being hospitalized since their last visit, and 7% report a cancer diagnosis. Five percent of the cohort reported having an STI diagnosis since their last study visit. The average time living with HIV for participants is 11 years. Stratification of the aforementioned variables by pain category can be seen in Table 3.1.

Association Between Pain and Viral Suppression

Table 3.2 presents the unadjusted and fully adjusted associations between experiencing moderate/severe pain and viral suppression status. Coefficients for controlled variables are displayed in the table but are not interpreted due to Table 2 Fallacy. Based on the confidence intervals of the unadjusted and fully adjusted models, there does not appear to be an association between pain and viral suppression status among the WLWH in our cohort. Table S2 displays the odds ratios from three distinct models, each progressively incorporating additional groups of confounders, allowing for the observation of changes in the coefficients as additional variables are controlled for. In Model A, which examines the association while controlling for demographic and socioeconomic variables, the adjusted odds ratio is 1.05 with a 95% confidence interval of (0.75, 1.47). In Model B which controls for all Model A variables as well as variables related to health status and pain medication use, we have an adjusted odds ratio of 1.01 and a 95 CI of (0.69, 1.45). Lastly, in Model C which includes all prior variables in Models A and B as well as health behavior variables such as reported substance use, we have an adjusted odds ratio of 1.02 with a 95% CI of (0.70, 1.48). Results from all three models, as reflected by the

confidence intervals, indicate no association between pain and viral suppression among the cohort of WLWH.

Modifying Role of Substance Use

Table 3.3 presents the crude and fully adjusted odds ratios for the analysis of the association between pain and viral suppression status, stratified by stimulant, heavy alcohol, cannabis, cigarette, and other substance use. Results indicate that none of the substances examined in this study modify the association between pain and viral suppression. While we did not observe an association between our variables among those who do and do not report stimulant use, the interaction term for stimulant use approached significance, suggesting a potential trend that may merit further study (p-value = .08). The moderate association indicated by the interaction coefficient could be attributed primarily to the influence of stimulant use, given that the aOR of the interaction term aligns closely with the aOR for the association between stimulant use and viral suppression when pain is held constant (aOR = 0.36, 95% CI [0.20, 0.66]). This suggests that, as we often see in literature, stimulant use is associated with viral suppression, independent of pain status. Figure 3.2 provides a visual representation of the effect of pain on viral suppression status stratified by stimulant use.

Discussion

The purpose of this study was to explore how experiences of moderate/severe pain among WLWH impacts their viral suppression status. We hypothesized that those living with pain may find activities such as medication adherence challenging due their pain status, and those challenges would intensify for WLWH who experience pain and report using legal and illegal substances. In our cohort of 1,418 WLWH, experiencing moderate to severe pain was not associated with lower odds of viral suppression. This suggests that while experiences of pain

have been shown to impact activities of daily living, such as medication adherence, our sample did not provide evidence of this. Our results differ from what is seen in recent literature, and this could be due to a number of reasons. One plausible explanation may lie in the unique context of HIV management, which necessitates rigorous, daily ART adherence in order to maintain a healthy immune system. Unlike conditions that do not require such structured treatment regimens, the crucial need to maintain consistent antiretroviral therapy could overshadow the disruptive effects of pain on daily activities, such as medication adherence. Consequently, even if pain affects aspects of daily living, the critical importance placed on adhering to their treatment in our study population might mitigate its potential impact on viral suppression. Samples seen in prior studies on the topic of pain, activities of daily living, and medication adherence include the general population,[148] individuals with musculoskeletal pain,[149] and those with rheumatic diseases,[150,151] which although all experience severe chronic pain, do not always require daily medication in order to maintain a functioning immune system.

Additionally, we could be seeing different results than what we find in literature due to sex differences in how women and men tolerate and function with pain. In a study examining the role of sex and gender in experiences of pain among 400 chronic spinal pain patients, results indicated that women reported higher levels of pain anxiety and intensity compared to men and yet despite experiencing more intense pain, women in the study displayed higher levels of daily functioning.[152] Similar results were seen in a study investigating sex differences in pain perception and coping strategies among 1,371 patients with chronic pain, where women demonstrated significantly higher levels of pain acceptance, activity level, and activity engagement compared to the men in study, even while exhibiting the same level of pain, severity of symptoms, and discomfort.[153]

Although no substance was shown to modify the association between pain and viral suppression among WLWH, we know that substance use, particularly stimulants, have been shown to adversely impact ART adherence among individuals living with HIV, independent of pain status. Stimulants, such as cocaine and methamphetamines, have been associated with multiple health complications, including inconsistent viral suppression and tryptophan degradation due to their effects on the immune system.[154-156] This results in impaired quality of life, neurocognitive impairments, and other mental health disturbances, which can further disrupt adherence to HIV treatment.[156,157]

Strengths

An important implication from our study is its contribution to future analyses and interventions. Our study is among a which focus on pain as an independent variable while examining its association with viral suppression among PLWH. Numerous studies have reported pain prevalence rates, predictors of pain, and pain as a dependent variable in various research questions,[158-160] however a limited number focus on the impact pain has on viral suppression, and even fewer focus on WLWH.[44,161-163] Results from this study may highlight appropriate areas to intervene on when trying to improve ART adherence among WLWH. Our findings suggest the necessity of focusing on individuals who report both pain and stimulant use, as stimulant use—whether in combination with pain or independent of it—significantly lowers the odds of viral suppression. Interventions aimed at addressing substance use have been shown to positively impact HIV outcomes such as healthcare utilization and ART adherence, therefore medical visits offer a crucial opportunity for intervention. Integrating substance use assessments and tailored intervention strategies into routine HIV care allows providers to proactively address these issues.[163-167] Additionally, future analyses would benefit from exploring this relationship

longitudinally to examine any changes in viral suppression over time as pain status fluctuates. This approach would provide deeper insights into the dynamic nature of the association between pain and viral suppression, and the moderating role of substance use in individuals living with HIV.

Our study also benefited from a diverse range of races and ethnicities and a robust sample size. While the number of WLWH who identify as Asian/Pacific Islander/Alaskan Native/American Indian/other remained comparatively small, 73% of our cohort consisted of individuals identifying as Black, and an additional 13% as Hispanic. This representation is particularly crucial given the historical underrepresentation of these groups in scientific research. Our diverse sample ensures that our conclusions are more generalizable across different demographic segments. Additionally, our large sample size aided our study as it enhanced the statistical precision of our findings. A larger sample size is instrumental in increasing the power of the study and reducing the likelihood of a type II error (a false negative conclusion), which enables more accurate effect estimates.

Limitations

In conducting this cross-sectional study on the association between self-reported pain and viral suppression among WLWH, several limitations have been identified. The inherent nature of cross-sectional designs restricts the ability to infer causality between pain and viral suppression, therefore, results only highlight the association between pain status and viral suppression. As previously mentioned, future studies would benefit from longitudinal examination which would allow for a more comprehensive assessment of the temporal dynamics and potential causal interactions between changes in pain status and variations in viral suppression over time.

As is common with most studies, there is a risk of uncontrolled confounding. However, from what was available in the dataset, appropriate confounders have been controlled for in the analysis to mitigate this risk. Lastly, the four-week data collection period for the pain variable may not accurately reflect the long-term impact of pain on viral suppression. Studies that can identify chronic pain among PLWH provide a more nuanced understanding of the sustained effects of pain on viral suppression outcomes. Additionally, such studies could explore differential impacts of chronic versus acute pain, potentially revealing important distinctions that could inform tailored interventions and management strategies.

Conclusion

In conclusion, this study investigated the relationship between moderate to severe pain and viral suppression among WLWH. Contrary to our initial hypothesis and existing literature, we found no significant association between pain and reduced viral suppression in our cohort. This suggests that the crucial need for consistent ART adherence in managing HIV might help mitigate any potential disruptions that pain could cause on medication-taking behaviors. Furthermore, our results highlight the complexity of pain's impact when intersected with factors like substance use, where stimulant use significantly compromised viral suppression. These findings underscore the need for tailored interventions that address both pain management and substance use to optimize HIV treatment outcomes. Future research should extend these findings through longitudinal studies to better understand the interplay between pain, substance use, and viral suppression over time, offering deeper insights into effective strategies for improving health outcomes in this vulnerable population.

Table 3.1. Participant characteristics at by pain.

	No/Mild Pain (*n*=926, 65%)		**Moderate/Severe Pain (*n*=492, 35%)**		**Total (*n*= 1,418)**	
	n/median	%/SD	*n/median*	%/SD	*n*	%
Demographics						
Age	49	8.8	50	9.2	49	9.0
Sexual Identity*						
Heterosexual	840	91.0	429	87.2	1,269	89.7
Gay or Lesbian	27	2.9	18	3.6	45	3.2
Bisexual	54	5.9	41	8.3	95	6.7
Other Sexual Orientation	2	0.2	4	0.8	6	0.4
Race & Ethnicity***						
Black	691	74.6	342	69.5	1,033	72.9
Hispanic	135	14.6	56	11.4	191	13.4
White	78	8.4	76	15.5	154	10.9
Asian/HPI/Native American/AN/Other	22	2.4	18	3.6	40	2.8
Education						
Below HS	305	33.0	173	35.2	478	33.7
HS Diploma/Equivalent	298	32.2	138	28.0	436	30.8
Some/Complete High Ed	322	34.8	181	36.8	503	35.5
Income**						
Above 200% FPL	248	27.4	100	20.7	348	25.1
Below 200% FPL	657	72.6	383	79.3	1,040	74.9
Employment***						
Employed	363	39.2	138	28.0	501	35.4
Unemployed	562	60.8	354	72.0	916	64.6
Insurance Coverage						
Insured	902	97.6	481	97.8	1,383	97.7
Uninsured	22	2.4	11	2.2	33	2.3
Substance Use						
Heavy Alcohol Use	104	11.2	45	9.2	149	10.5
Cannabis Use**	152	16.5	117	23.8	269	19.0
Current Cigarette Use	349	37.7	203	41.3	552	38.9
Stimulant Use*	46	5.0	37	7.5	83	5.9
Other Substance Use**	16	1.7	18	3.6	34	2.4
Polysubstance Use	20	2.2	14	2.9	34	2.4
Health Status						
STIs*	41	4.4	33	6.7	74	5.2
Depression***	201	21.8	228	46.4	430	30.4
Years Living With HIV	11.4	7.4	11.5	8.1	11.4	7.7
Hospitalized***	166	19.2	171	36.7	337	25.2
Cancer History	59	6.4	38	7.7	97	6.8
Pain Medication Use***	688	74.3	449	91.5	1,137	80.2
Virally Suppressed	788	86.1	422	86.5	1,210	86.2

*$0.05 \leq p < 0.1$; **$0.001 \leq p < 0.05$; ***$p < 0.001$.

Table 3.2. Estimated unadjusted and adjusted odds ratios (ORs) with 95% CI for the analysis of the association between viral suppression and pain.

Variables	Unadjusted:			Adjusted:		
	OR	P-Value	(95% CI)	aOR[1]	P-Value	(95% CI)
Pain	1.03	0.85	(0.74, 1.42)	1.02	0.90	(0.70, 1.49)
Cannabis Use	-	-	-	0.79	0.39	(0.46, 1.35)
Heavy Alcohol Consumption	-	-	-	0.61	0.10	(0.33, 1.10)
Stimulant Use	-	-	-	0.59	0.27	(0.25, 1.37)
Cigarette Use	-	-	-	0.82	0.40	(0.52, 1.29)
Other Substances	-	-	-	1.20	0.82	(0.23, 6.14)
Age at Visit	-	-	-	1.04	<0.00	(1.02, 1.07)
Income[2]	-	-	-	1.00	0.97	(0.63, 1.59)
Education						
< High School (HS)	-	-	-	-	-	-
HS/Equivalent	-	-	-	1.10	0.64	(0.72, 1.69)
Advanced Degree	-	-	-	0.85	0.46	(0.55, 1.30)
Employment[3]	-	-	-	1.17	0.45	(0.77, 1.78)
Race/Ethnicity						
White	-	-	-	-	-	-
Black	-	-	-	0.84	0.57	(0.46, 1.53)
Hispanic/Latinx	-	-	-	1.09	0.80	(0.52, 2.32)
Asian/HPI/NA/AN/Other	-	-	-	0.82	0.72	(0.27, 2.48)
Depression	-	-	-	0.85	0.41	(0.58, 1.24)
Years Living with HIV	-	-	-	0.96	0.01	(0.94, 0.99)
Hospitalized	-	-	-	0.85	0.45	(0.57. 1.28)
Cancer History	-	-	-	1.09	0.80	(0.53, 2.26)
STI Diagnosis	-	-	-	1.01	0.97	(0.49, 2.08)
Pain Medication Use	-	-	-	1.48	0.05	(0.99, 2.23)

[1]aOR: adjusted odds ratio. [2]Income refers to those whose median annual salary is less than 200% of the Federal Poverty Limit.
[3]Employment includes both part-time and full-time positions.

Table 3.3. Post-estimation Odds Ratios for the analysis of the association between viral suppression and pain by substance use category.

	Crude Odds Ratio (95% CI)		**Adjusted** Odds Ratio (95% CI)		P for Interaction*
	Stimulants Use	No Stimulants	Stimulants Use	No Stimulants	
Pain Mod/Severe vs No/Mild	0.57 (0.23, 1.44)	1.18 (0.83, 1.68)	0.43 (0.15, 1.22)	1.16 (0.77, 1.75)	.08
	Alcohol Use	No Alcohol	Alcohol Use	No Alcohol	
Pain Mod/Severe vs No/Mild	0.75 (0.34, 1.67)	1.07 (0.75, 1.52)	0.92 (0.38, 1.24)	1.04 (0.69, 1.56)	0.80
	Cannabis Use	No Cannabis	Cannabis Use	No Cannabis	
Pain Mod/Severe vs No/Mild	0.92 (0.51, 1.68)	1.15 (0.78, 1.70)	0.90 (0.46, 1.74)	1.08 (0.69, 1.68)	0.64
	Cigarette Use	No Cigarette	Cigarette Use	No Cigarette	
Pain Mod/Severe vs No/Mild	0.82 (0.52, 1.29)	1.34 (0.84, 2.14)	0.87 (0.52, 1.47)	1.18 (0.71, 1.97)	0.41
	Other Substance	No Other Sub.	Other Substance	No Other Sub.	
Pain Mod/Severe vs No/Mild	1.59 (0.34, 7.37)	1.02 (0.73, 1.42)	0.79 (0.10, 6.01)	1.03 (0.70, 1.51)	0.8

*The P for Interaction is from the fully adjusted model that includes an interaction term.

Figures

Figure 3.1. Directed Acyclic Graph Demonstrating Association Between Pain and Viral Suppression and the Potentially Modifying Role of Substance Use

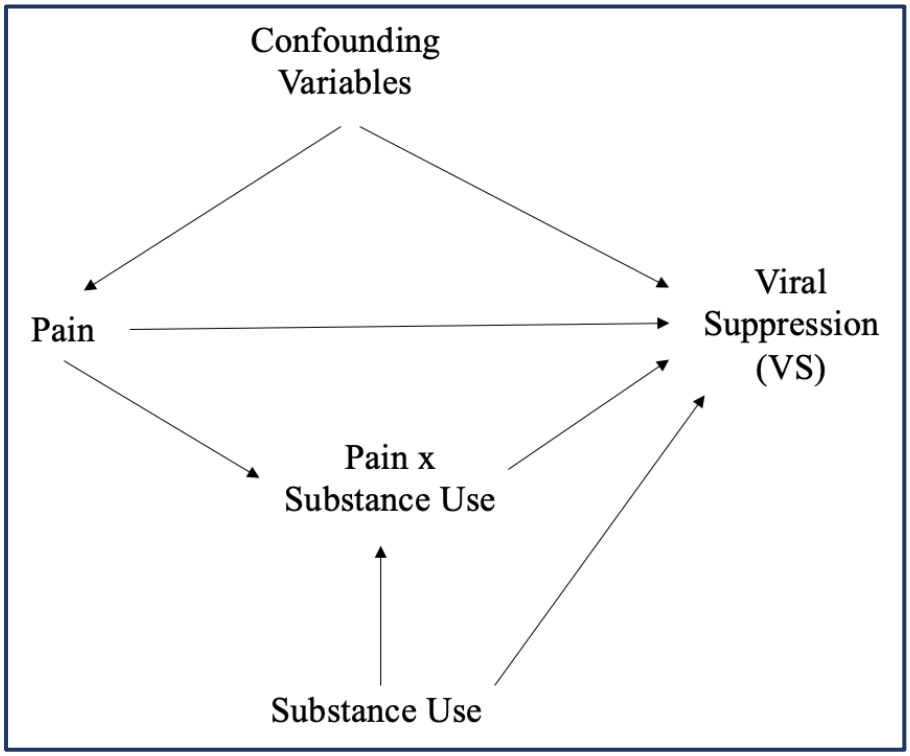
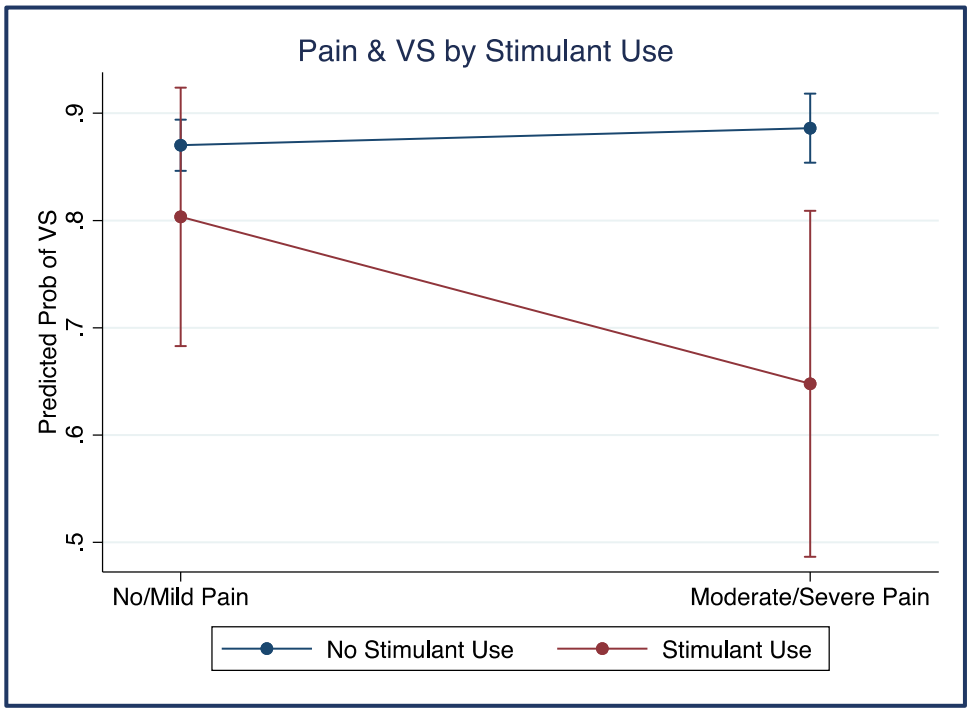


Figure 3.2. The effect of pain on viral suppression, stratified by stimulant use.



Chapter IV. Study 3: Navigating Health and Happiness: Quality of Life and Viral Suppression Among Women Living With HIV.

Abstract

Background: Despite significant advancements in antiretroviral therapy (ART), public health institutions continue to prioritize efforts to enhance ART adherence and increase the rates of viral suppression among people living with HIV. Quality of life, encompassing physical health, psychological well-being, and socioeconomic stability, has been consistently linked to better adherence to antiretroviral therapy (ART) and, subsequently, viral suppression. This study focuses on understanding how the quality of life is associated with viral suppression among women living with HIV (WLWH), while also considering the impact of racial and ethnic disparities.

Methods: The study utilized data from the Women's Interagency HIV Study (WIHS) cohort, spanning from 2014 to 2018. To assess the relationship between quality of life and viral suppression, as well as potential disparities by race and ethnicity, mixed-effects regression models were used. Models were adjusted for a comprehensive set of variables, including socioeconomic factors, mental health conditions, and other health behaviors.

Results: Results demonstrated a significant positive association between quality of life and viral suppression (aOR: 1.17, 95% CI [1.10, 1.25]). However, the magnitude of this association was shown to vary by racial and ethnic group. The increase in odds of viral suppression per one-point rise in quality of life score was greatest among White WLWH and least among Black WLWH.

Conclusion: These findings highlight the significant association between quality of life and viral suppression in WLWH. They also reveal racial and ethnic disparities, suggesting the need for

tailored interventions that address both the personal and systemic factors affecting health outcomes among diverse populations of women.

Keywords: HIV; Quality of Life; Racial and Ethnic Disparities; Viral Suppression

Background

Viral Load and Well-Being

The successful management of HIV/AIDS hinges on the delicate balance between achieving viral suppression and enhancing an individual's quality of life.[168] Viral suppression, a critical goal in the management of HIV, is achieved when antiretroviral therapy (ART) effectively lowers the viral load in a patient's blood to <200 copies/ml.[104] Achieving and maintaining viral suppression is paramount not only for the health of the individual but also for public health, as it significantly reduces the risk of HIV transmission.[28,104] However, the journey towards consistent viral suppression is multifaceted and influenced by a myriad of factors, one of which is the individual's perceived quality of life.[169,170]

Quality of Life Factors and Viral Suppression

Quality of life encompasses a broad spectrum of personal experiences, including physical health, psychological state, history of trauma, and socio-economic factors.[171,172] In the context of PLWH, these dimensions of quality of life can play a pivotal role in influencing clinical outcomes.[46,173] Numerous longitudinal studies demonstrate the association between mental health issues such as depression and post-traumatic stress disorder (PTSD), and negative HIV outcomes.[32,174,175] PLWH who report depressive symptoms or PTSD are more likely to have a detectible viral load (≥75 copies/mL) and lower CD4 cell counts.[60,175,176] Similarly, PLWH who experience trauma or intimate partner violence are less likely to be virally suppressed compared to those with no history of trauma or physical/sexual violence.[177,178] Lastly, socioeconomic factors such as housing status have been shown to be determinants of HIV health outcomes. PLWH who are permanently housed have a higher proportion of viral suppression compared to their unhoused counterparts.[179] In addition, PLWH who currently live in stable housing are more

likely to achieve a CD4 cell count ≥ 500 cells/mm³, indicating a robust immune response compared to PWLH in unstable housing.[179,180] This is likely due to barriers to accessing healthcare and medication adherence, which is crucial for viral suppression. PLWH without stable housing may struggle with ART adherence due to psychological stress and competing priorities for survival, such as the inability to meet food and hygiene needs.[181,182] These diverse factors that can shape an individual's perception of their quality of life — mental health status, history of trauma, and socioeconomic status — interact intricately, each significantly impacting the viral suppression in PLWH.

Quality of Life Among Women

In exploring the unique challenges to viral suppression, it becomes evident that women are more frequently affected by specific factors that can significantly shape their perceived quality of life, such as experiences of intimate partner violence (IPV), trauma, and depression.[183-185] These factors collectively create a complex web of psychological and social hurdles that significantly impede women's well-being and life satisfaction. IPV, a pervasive issue affecting women globally, not only poses immediate physical risks but also leads to long-term psychological trauma, undermining their sense of security and self-worth.[186] This trauma, often compounded by societal stigma and inadequate support systems, escalates the risk of developing mental health disorders, with anxiety being notably prevalent among affected women.[187] Such mental health challenges further exacerbate the struggle to maintain or improve quality of life, as they can lead to social withdrawal, reduced workforce participation, and diminished ability to engage in positive health behaviors.[188-190] Similar effects can be seen among individuals living with depression. People experiencing depression often face a decline in their overall quality of life.[191] This is due to a combination of factors such as persistent sadness, feelings of

worthlessness, and a general lack of energy or motivation.[192] These factors can, in turn, impact their adherence to ART regimens, a key determinant of viral suppression.[193]

Quality of Life Among Racial/Ethnic Minority Women

Upon further examining subgroups within WLWH, it becomes clear that understanding the factors impacting viral suppression among racial/ethnic minority women requires a broader perspective where we consider factors beyond the conventional domains that are seen to be associated with viral suppression. While we know that mental health issues and socioeconomic status can influence an individual's ability to adhere to their medication and access healthcare, there are unique issues that racial/ethnic minority women experience that become additional barriers to achieving viral suppression.[194-196] One example is the structural racism, discrimination, and stigma women of color are subjected to, which numerous studies have liked to trauma, psychological distress, and lower levels of healthcare utilization.[195,197-200] Physician bias and racial stereotypes have also been linked to disparities in the quality of care received by racial/ethnic minority women compared to their white counterparts.[201] This situation is compounded by a lack of culturally competent healthcare practices, where a disconnect between healthcare providers and the unique cultural experiences of these women hampers effective communication and trust, crucial for treatment adherence and viral suppression.[202] Therefore, when exploring factors impacting viral suppression among racial/ethnic minority women, there are variables beyond income, depression, and employment that may be hindering their ability to adhere to their HIV medication, and thus reach viral suppression.

Investigating the impact of quality of life on viral suppression among WLWH and examining differences by racial and ethnic minority status is an important key for developing equitable, effective, and personalized healthcare solutions in HIV management. This

intersectional approach recognizes that social and behavioral determinants, such as substance use and socioeconomic conditions, often have a differential impact on various racial groups. These determinants, coupled with unique cultural and behavioral factors inherent to each racial or ethnic group, can significantly influence health outcomes, including adherence to HIV treatment regimens. Understanding these disparities is crucial for developing targeted and culturally sensitive interventions, thereby contributing to the reduction of health inequities among different racial and ethnic populations.

Methods

Sample and Study Design

The study sample employed in this analysis is consistent with the one detailed in the preceding chapter, however, the current study will utilize longitudinal data from participants enrolled in the WIHS cohort from 2014 to 2018 across all sites. The visit numbers corresponding to these dates are: 40 – 48, where $Time_1$ = visit 40. The primary study visits are conducted on an annual basis, where information on medical history substance use, sexual behavior, health care utilization, and psychosocial and behavioral factors are collected during the study visit. In addition to data collected via interviews, participant blood, urine, and cervicovaginal swabs are also collected for testing.

Variables

Dependent Variable:

Our primary outcome is viral suppression. Viral load <200 copies/ml will be identified as virally suppressed and viral load >200 copies/ml will be labeled as not virally suppressed. Viral load is measured using the Abbot m2000 HIV-1 RealTime System at the time of each study visit.

Independent Variable:

Participant-reported quality of life is the primary predictor of interest. WIHS participants report their overall rating of their quality of life on a scale of 0 – 10, with a score of 10 representing the highest quality of life and 0 representing the lowest quality of life.

Moderating Variable:

The moderating variable is race and ethnicity. Ethnicity was identified through self-reported data, following the categorization guidelines of the US Census. Participants initially specified their race from options including White, Black, Asian, American Indian/Alaska Native, Pacific Islander, Native Hawaiian, or "other." Subsequently, they were asked to indicate whether they identified as Hispanic. Based on these responses, we created White (non-Hispanic), Black (Non-Hispanic), Hispanic/Latinx, and Asian/HPI/Native American/AN/Other categories.

Confounders/Additional Variables:

Time-varying covariates include depression (defined as having scores ≥16 using the Center for Epidemiologic Studies Depression (CES-D) scale),[147] employment status (Employed, Unemployed, or Unknown), health insurance (Insured or Uninsured), years living with HIV (number of years since participant first tested seropositive for HIV), heavy alcohol consumption (defined per CDC guidelines for women),[146] current cigarette smoking status (Not smoking or Smoking), marijuana use (defined as using marijuana since last study visit), any substance use since last visit (Yes if participant has used the following substances since their last study visit: Cocaine, heroin, illicit methadone, amphetamines, injection drugs, non-injected recreational drugs (hallucinogens), methamphetamines), any STI diagnosis (Yes if participant tested positive for Gonorrhea, Syphilis, Chlamydia, PID, Genital Herpes, Genital Warts, Trichomonal Vaginitis, Bacterial Vaginitis), cancer diagnosis (Yes if participant reports having a history of cancer

diagnosis), medical incidents (Yes if participant reports diagnosis of angina/heart disease, congestive heart failure, heart attack, stroke, transient ischemic attack, or tuberculosis), and pain (Yes if participant reported “Moderate”, “Severe”, and “Very Severe” pain in the last 4 weeks). A polysubstance use variable was also created to capture participants who report using more than two substances since their last visit. A time variable was creating using visit numbers, where visit #40 is identified as Time 0.

Time-fixed covariates include education level at time of visit 40 (Below high school (HS), some HS diploma/equivalent, some/completed higher education), age at time 0 (years), and sexual orientation (Heterosexual, Gay, Bisexual, Other).

Inclusion/Exclusion Criteria

The study population will consist of seropositive women who were under observation in the WIHS cohort. Serostatus is verified using documentation of a reactive HIV blood serum and confirmatory test and reported having been prescribed ART at any study visit.

Data Analysis

The analyses were performed using STATA 16.[100] Interpretation of statistical significance was guided by confidence intervals. The distribution of the variables of interest was assessed to identify influential observations/outliers, skewness, and missing data. Means (SD) and frequencies (percentage) were calculated to describe the sociodemographic characteristics of the patients at Time 0. The variables described above were compared by viral suppression status using Pearson’s chi-square tests for categorical variables and two-sample t-tests for continuous variables. Missing data was minimal in the study. Viral load data was missing for 1.26% of our sample (n=17). Missing data for the self-reported quality of life score (n=18, 1.34%), income (n=270, 3.68%), education (n=5, 0.07%), depression diagnosis (n=72, 0.98%), illegal substance

use (n=30, 0.41%), cannabis use (n=32, 0.44%), alcohol consumption (n=30, 0.41%), and STI diagnosis (n=20, 0.27%) were minimal. Thus, we conducted a complete case analysis. A full list of variables and their missing data is seen in Table S3.

Given the longitudinal nature of the data, mixed-effects regression models were used to account for the correlation between repeated measures, allowing for the examination of between-subjects and within-subject effects. We ran unadjusted and adjusted mixed-effects regression models to assess the association between participant quality of life and viral suppression status over time. Adjusted models control for potential covariates such as income, depression, and any substance use since their last study visit. The models will include a subject-level random effect to account for correlated repeated measures within each individual and a site-level random effect to account for any similarities among participants by recruitment site. The fixed effects will include quality of life score, substance use, depression status, socio-demographics, and time. The model will include an interaction between quality of life and time to observe any changes in the association over time. We will further add an interaction term to examine whether there are disparities in the association between quality of life and viral suppression by racial/ethnic minority status over time.

Results

Demographic and Socioeconomic Characteristics

At time 0, the overall cohort had an average age of 48 years (SD = 9.2, range [25 – 79]). Approximately 90% of the cohort identify themselves as heterosexual; 16% as Hispanic, 70% as Black/African-American, and 11% as White. More than 94% of the cohort hold health insurance coverage, and 74% earn an income below 200% of the federal poverty limit (less than $2,000 per month). Sixty-eight percent are unemployed, with roughly equal numbers of participants having

below a high school education, a high school education or equivalent degree, and an advanced degree (33.7%, 32.1%, 34.2% respectively).

Health Behaviors

Thirty nine percent of the cohort are current cigarette smokers, 18.5% have smoked marijuana since their last visit, and almost 11% report heavy alcohol consumption as defined by the CDC.[146] Twenty two percent report illegal substance use and 3.3% report using more than two illegal substances since their last visit.

Health Status

Thirty-one percent of the WLWH in the cohort meet the diagnostic criteria for depression. The cohort members have lived with HIV for an average of 16 years, and 8% report a history of cancer diagnosis. Thirty-three percent of the cohort report experiencing moderate to severe pain in the last four weeks and 81% of the cohort were virally suppressed. Table 4.1 shows the stratification of these variables by viral suppression status at time 0 and Figure 4.3. demonstrates the changes in viral suppression over time.

The regression analysis demonstrated that an increase in the quality of life score is significantly associated with higher odds of achieving viral suppression, as evidenced in both the unadjusted and fully adjusted models presented in Table 4.2. Adjusting for demographic and socioeconomic characteristics, health behaviors, health status, and time, each unit increase in the quality of life score is associated with a 17% increase in the odds of achieving viral suppression (aOR: 1.17, 95% CI [1.10, 1.25]).

Table S4 demonstrates the multi-model approach used to investigate the impact of quality of life on viral suppression among the cohort of women living with HIV. Model A, adjusting for time, demographic, and socioeconomic variables, revealed that each unit increase in the quality

of life score was associated with a 20% increase in the odds of achieving viral suppression (aOR 1.20, 95% CI [1.13, 1.28]). Model B, which further accounted for variables related to health status and health behaviors, yielded a consistent association (aOR 1.18, 95% CI [1.10, 1.26]). In Model C, the most comprehensive model including all variables from Models A and B as well as an interaction term between race/ethnicity and quality of life, the positive relationship between quality of life and viral suppression remained (aOR 1.17, 95% CI [1.10, 1.25]).

Time is also shown to be associated with viral suppression, as seen in Figure 3, where we see higher proportion of WLWH who are virally suppressed as time progresses. Compared to Time 0, the odds of viral suppression among women in the cohort is greater at Times 1-4 (Time 1: aOR 1.36, 95% CI [1.04, 1.77], Time 2: aOR 1.88, 95% CI [1.43, 2.47], Time 3: aOR 2.32, 95% CI [1.7, 30.9], Time 4: aOR 2.39, 95% CI [1.78, 3.20]).

While the mixed effects model demonstrated a positive association between odds of viral suppression and quality of life score, when examining racial and ethnic disparities in the association of interest, we find that the odds of viral suppression per one-point increase in quality of life score among Black woman is 22% less than their White counterparts. Similar results are seen among Hispanic women (aOR 0.78, 95% CI [0.58, 1.04]) where we find a smaller increase in odds of viral suppression per each unit increase in quality of life score. Due the small sample size, the Asian/Pacific Islander/Alaskan Native/American Indian effect estimates will not be interpreted but are displayed in Table 4.3.

In order to explore the association of quality of life on viral suppression among the racial/ethnic categories, we utilized a nonlinear combination of estimators via the nlcom command in STATA.[100] This command was used to calculate the exponentiated coefficients of the quality of life score by race/ethnicity. By exponentiating the regression coefficients we

transform them from a log-odds scale to an odds ratio scale, which is more interpretable in the context of our logistic regression model. The estimated odds ratios for each racial/ethnic category are seen in Table 4.4. The greatest increase in odds of viral suppression per one-point increase in quality of life score is seen among White WLWH (aOR 1.49, 95% CI [1.14, 1.82]). Black WLWH also demonstrate an increase in the odds of viral suppression per one-point increase in quality of life score, however, this rise is observed at a lower rate compared to their White counterparts, with a 16% increase versus a 49% increase per unit increase in quality of life score. A moderate increase in odds of viral suppression is seen among Hispanic women living with HIV (aOR 1.16, 95% CI [0.95, 1.38]). As previously mentioned, the effect estimates for WLWH who identify as Asian/Pacific Islander/Alaskan Native/American Indian/other are not interpreted due to sample size issues but are displayed in Table 4.4. The predicted probabilities of viral suppression at various quality of life by race/ethnicity have been graphed and displayed in figure 4.4.

Discussion

The purpose of this study was to explore the relationship between self-reported quality of life and viral suppression status among WLWH and examine any discrepancies in this association across different racial and ethnic groups. We hypothesized that improvements in self-reported quality of life would correspond to increased odds of viral suppression. Due to the experiences of racism within the healthcare system and historical medical mistrust among communities of color, we further hypothesized that the increase in odds of viral suppression would be most significant among White WLWH and least among Black WLWH. In our cohort, every one unit increase in quality of life score increased odds of viral suppression among WLWH. This trend was seen among all racial and ethnic groups, however, as hypothesized, the

greatest increase was seen among White women and the smallest increase was among the Black women in the cohort. This suggests that one's quality of life, which encompasses various physical, psychological, and socioeconomic factors, can impact viral suppression status. In addition, the observed differences in the association between quality of life and viral suppression across racial and ethnic groups suggest the presence of underlying factors that may influence these disparities. These results are mirrored in other studies and research has identified several pathways that could explain this relationship.[203-205]

One explanation involves the demonstrated correlation between higher quality of life and factors such as mental health status and social support, both of which have been shown to be associated with adherence to ART and in turn viral suppression.[206] Mental well-being can reduce the incidence of depressive symptoms, a known barrier to consistent medication adherence.[207] Additionally, robust and supportive social networks may provide emotional and practical support, such as reminders to take medications and transportation to clinic appointments, which can further improve adherence rates.[208,209] Moreover, socioeconomic status, a critical component of quality of life, represents one of the pathways through which quality of life could influence viral suppression. Individuals with higher socioeconomic status typically have better access to healthcare resources and less economic stress, factors that facilitate regular engagement with healthcare services and adherence to treatment protocols.[210-212]

Our results also demonstrated racial and ethnic disparities in the impact of quality of life on viral suppression, particularly among Black women compared to their White counterparts, which highlights a deeper systemic issue within healthcare. These disparities could be partially attributed to racism in the healthcare system and the resultant medical mistrust prevalent in communities of color.[213] Historical and ongoing discrimination in medical settings contributes to

a lack of trust towards healthcare providers, which can significantly deter regular engagement with HIV treatment services and adherence to ART.[197,214] Black women living with HIV may face multiple barriers including inadequate access to culturally competent care, stigma associated with HIV within their communities, and economic inequalities that limit their ability to maintain consistent treatment.[215,216] Furthermore, systemic bias in the healthcare system often results in less personalized care and suboptimal management of comorbidities for women of color.[217] These inequities could explain why improvements in quality of life do not translate as effectively into better health outcomes for racial and ethnic minority women as they do for White WLWH.

Strengths

This study leverages several key strengths. Primarily, its longitudinal design enables the observation of trends providing a perspective on how individuals' perceptions of their quality of life changes over time and how that impacts their viral suppression. Additionally, the substantial sample size increases the precision of the estimates, thereby reducing the margin of error and enhancing the credibility of the results.[218] Study results from large a cohort enables a more accurate generalization of the findings to the broader population, reducing the likelihood of statistical anomalies and biases that often affect studies with smaller cohorts.

Another significant methodological strength of this study is the use of self-reported quality of life scores. Unlike calculated scores that might inadvertently impose a normative assessment based on socioeconomic and health-related variables, self-reported measures respect individual perceptions and subjective experiences. This approach acknowledges that quality of life is a deeply personal construct, influenced by factors beyond mere economic or health statuses. For example, someone with health issues or a low-income individual might still report a high quality of life due to strong social support, personal resilience, or other compensatory

factors. By using self-reported measures, our study more accurately captures the complex and multifaceted nature of quality of life as experienced and interpreted by individuals themselves, offering insights that are more aligned with the subjective well-being and actual lived experiences of the study participants.

Limitations

One notable limitation of our study is the underrepresentation of individuals from certain ethnic backgrounds, including Asian, Pacific Islander, Alaskan Native, and American Indian. This lack of diversity may limit the generalizability of our findings to these populations. Studies have shown that different ethnic groups can exhibit varying health outcomes and interactions with healthcare systems, which might not be adequately captured in our research due to this underrepresentation. Another limitation arises from potential uncontrolled confounding variables that were not accounted for in the study design. While our analysis attempts to explore the longitudinal association between quality of life scores and viral suppression among individuals living with HIV, there may be additional factors that could influence these outcomes and if not controlled for, may lead to biased results and misinterpretations of the relationship. Building off this limitation, examining factors such medical mistrust and experiences of racism within healthcare settings would be beneficial to examine alongside the discrepancies in the association that we saw in the association by race/ethnicity. Medical mistrust and experiences of racism can significantly deter individuals from accessing healthcare services which is essential for effective viral suppression. Investigating these elements could provide more comprehensive insights into why these disparities exist and how they can be addressed to improve health equity.

Finally, the geographical scope of the study, limited to a handful of states, poses a limitation. This restriction potentially overlooks the variability in stigma and criminalization

laws against PLWH that differ significantly across the United States. A more nationally representative sample, including states with diverse legal and social climates regarding HIV, would provide a more comprehensive understanding of the impact of these factors on the quality of life and viral suppression.

Conclusions

This study focused on the influence of quality of life on viral suppression among women living with HIV, with a particular emphasis on the differences observed across various racial and ethnic groups. The findings revealed that an increase in quality of life scores correlated with higher odds of achieving viral suppression. These findings underscore the role of quality of life—influenced by factors such as socio-economic status, mental health, and social support—in effectively managing HIV.

However, the data also uncovered notable disparities in this relationship based on race/ethnicity, particularly between Black women and their White counterparts. This suggests that deeper, systemic issues within healthcare systems may disproportionately affect non-White individuals, potentially impacting their ability to achieve viral suppression. Future research should focus on in-depth investigations into the specific factors contributing to these differences. A critical area of exploration could involve understanding how systemic racism and medical mistrust influence healthcare interactions and outcomes. Research could evaluate interventions designed to improve healthcare provider cultural competence and trust-building practices, which are crucial for increasing engagement with HIV treatment among racial and ethnic minority groups.

Also, expanding our analysis to incorporate broader and more diverse geographical areas could provide insights into how regional differences in healthcare access and stigma impact

quality of life and viral suppression. Stigma associated with HIV can significantly influence individuals' willingness to seek and adhere to treatment due to fear of discrimination or social exclusion. This stigma can manifest differently across various states and neighborhoods, influenced by cultural, social, and legal factors that either exacerbate or lessen discriminatory practices.

These insights are crucial for refining current models of healthcare delivery and interventions tailored to diverse populations. Tailoring strategies to meet the distinct needs of different demographic groups ensures that healthcare solutions are not only inclusive but also more responsive to the specific circumstances that influence health outcomes. This approach not only optimizes treatment efficacy but also fosters a more equitable healthcare environment where every individual has the best possible chance of managing their HIV effectively.

Tables

Table 4.1. Participant characteristics by viral suppression status at time = 0.

	Not Virally Suppressed (*n*=252, 19%)		**Virally Suppressed (*n*=1,072, 81%)**		**Total (*n*= 1,324)**	
	n/median	%/SD	*n/median*	%/SD	*n*	%
Demographics						
Age***	45	8.9	49	8.8	48	9.0
Sexual Identity						
Heterosexual	222	88.1	966	90.4	1,188	89.9
Gay or Lesbian	11	4.4	30	2.8	41	3.1
Bisexual	18	7.1	69	6.4	87	6.6
Other Sexual Orientation	1	0.4	4	0.4	5	0.4
Race & Ethnicity***						
Black	187	74.2	729	68.0	916	69.2
Hispanic	37	14.7	176	16.4	213	16.1
White	23	9.1	127	11.9	150	11.3
Asian/HPI/Native American/AN/Other	5	2.0	40	3.7	45	3.4
Education						
Below High School (HS)	90	35.9	356	33.2	446	33.7
Some HS Diploma/Equivalent	81	32.3	344	32.1	425	32.1
Some/Completed Higher Ed.	80	31.8	372	34.7	452	34.2
Income**						
Above 200% FPL	49	20.9	285	27.6	334	26.3
Below 200% FPL	186	79.1	749	72.4	935	73.7
Employment**						
Employed	65	25.9	362	33.8	427	32.3
Unemployed	186	74.1	708	66.2	894	67.7
Insurance Coverage***						
Insured	218	87.9	1,025	96.1	1,243	94.5
Uninsured	30	12.1	42	3.9	72	5.5
Substance Use						
Heavy Alcohol Use**	39	15.8	110	10.3	149	11.3
Marijuana use	54	21.9	186	17.4	240	18.2
Current Cigarette Use***	126	50.0	389	36.3	515	38.9
Any Substance Use**	70	28.3	220	20.5	290	22.0
Polysubstance Use***	19	7.54	24	2.2	43	3.3
Health Status						
STIs**	29	11.6	71	6.6	100	7.6
Depression*	88	35.7	318	29.9	406	31.0
Years Living With HIV***	14.8	7.5	16.1	7.2	15.8	7.3
Cancer History	16	6.3	88	8.2	104	7.9
Medical Incident	3	1.2	10	0.9	13	1.0
Moderate/Severe Pain	92	37.7	344	32.4	436	33.4

*$0.05 \leq p < 0.1$; **$0.001 \leq p < 0.05$; ***$p < 0.00$.

Table 4.2. Estimated crude and adjusted odds ratios (ORs) with 95% CI for the analysis of the association between viral suppression and quality of life score.

Characteristics	Crude Model:			Adjusted Model:		
	OR	(95% CI)	p-value	aOR	(95% CI)	p-value
Quality of Life Score	1.18	(1.12, 1.26)	<0.000	1.17	(1.10, 1.25)	<0.000

aOR: adjusted odds ratio. The adjusted model controls for all the variables in the unadjusted model as well as variables related to demographics, socioeconomic status, time, health status, and health behaviors. [§] Illicit substance use includes cocaine, crack, heroin, methamphetamines, amphetamines, injection drugs, non-injected recreational drugs, use of prescription drugs in a way not as prescribed, tranquilizers.

Table 4.3. Estimated odds ratios (ORs) for the analysis of the association between viral suppression and quality of life including an interaction term with race/ethnicity.

Characteristics	Unadjusted:			Fully Adjusted:		
	OR	(95% CI)	p-value	aOR	(95% CI)	p-value
Quality of Life Score	1.52	(1.22, 1.88)	<0.000	1.48	(1.18, 1.87)	0.001
Race/Ethnicity						
White	-	-	-	-	-	-
Black	3.21	(062, 16.27)	0.16	3.46	(0.63, 19.11)	0.15
Hispanic/Latinx	4.12	(0.51, 32.11)	0.18	5.36	(0.61, 47.12)	0.13
Asian/HPI/NA/AN/ Other	0.83	(2.22, 626.25)	0.01	37.1	(1.88, 733.6)	0.01
Race/Ethn. x QOL						
White	-	-		-	-	
Black	0.77	(0.62, 0.97)	0.02	0.78	(0.62, 0.99)	0.04
Hispanic/Latinx	0.80	(0.61, 1.06)	0.12	0.78	(0.58, 1.04)	0.10
Asian/HPI/NA/AN/ Other	0.56	(0.38, 0.81)	0.002	0.57	(0.38, 0.85)	0.006
Age at First Visit				1.07	(1.05, 1.10)	0.001
Income (<200% FPL)				1.03	(0.76, 1.40)	0.82
Education						
< High School (HS)				-	-	-
HS/Equivalent				1.29	(0.86, 1.93)	0.21
Advanced Degree				1.44	(0.96, 2.17)	0.07
Time						
Zero (Visit 40)				-	-	-
One (Visit 42)				1.38	(1.04, 1.82)	0.02
Two (Visit 44)				1.82	(1.36, 2.42)	<0.000
Three (Visit 46)				2.19	(1.62. 2.96)	<0.000
Four (Visit 48)				2.28	(1.68, 3.11)	<0.000
Depression				0.85	(0.65, 1.12)	0.26
Years Living with HIV				0.99	(0.96, 1.01)	0.53
Cancer History				1.07	(0.53, 2.11)	0.84
Illegal Substance Use[§]				0.48	(0.35, 0.64)	<0.000
Heavy Drinking				0.72	(0.50, 1.02)	0.07

aOR: adjusted odds ratio. Unadjusted model only includes race/ethnicity, quality of life score, and an interaction term between the two variables. The fully adjusted model controls for all the variables in the unadjusted model as well as variables related to demographics, socioeconomic status, time, health status, and health behaviors. [§] Illegal substance use includes cocaine, crack, heroin, methamphetamines, amphetamines, injection drugs, non-injected recreational drugs, use of prescription drugs in a way not as prescribed, tranquilizers.

Table 4.4. Post-Estimation calculation of odds ratio (ORs) with 95% CI for the analysis between viral suppression and quality of life score stratified by racial/ethnic group.

	White	Black	Hispanic	Asian/PI/AN/AI
	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
QoL	1.49 (1.14, 1.82)	1.16 (1.08, 1.25)	1.16 (0.95, 1.38)	0.85 (0.58, 1.12)

QoL: Self-reported quality of life score. PI: Pacific Islander. AN: Alaskan Native. AI: American Indian.

Figures

Figure 4.1. Simplified Directed Acyclic Graph Demonstrating Relationship Between Quality of Life and Viral Suppression

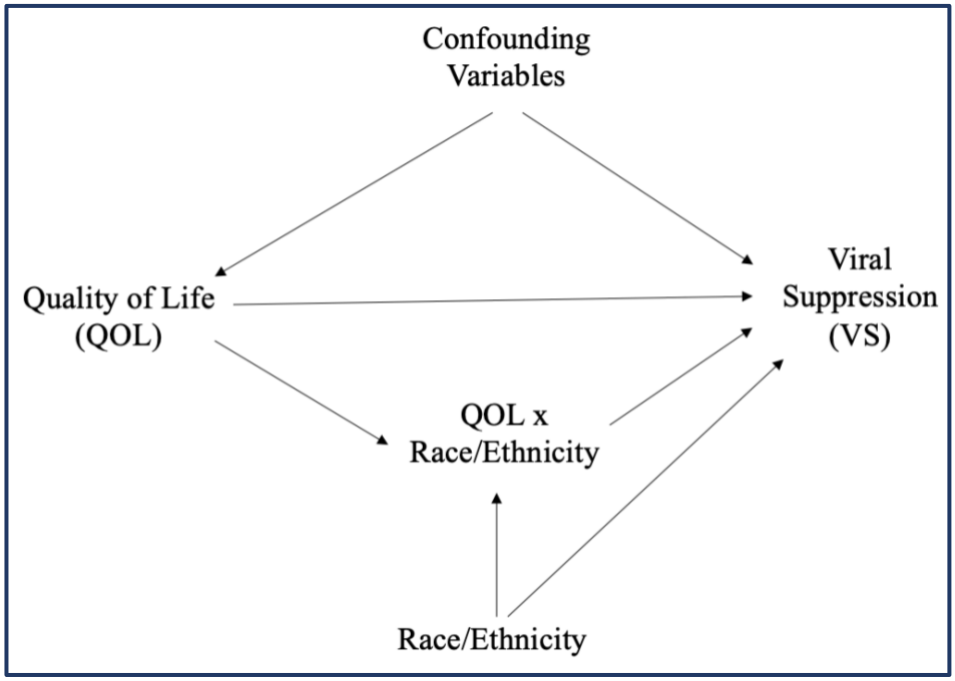


Figure 4.2. Time-Varying Directed Acyclic Graph Demonstrating Relationship Between Quality of Life and Viral Suppression

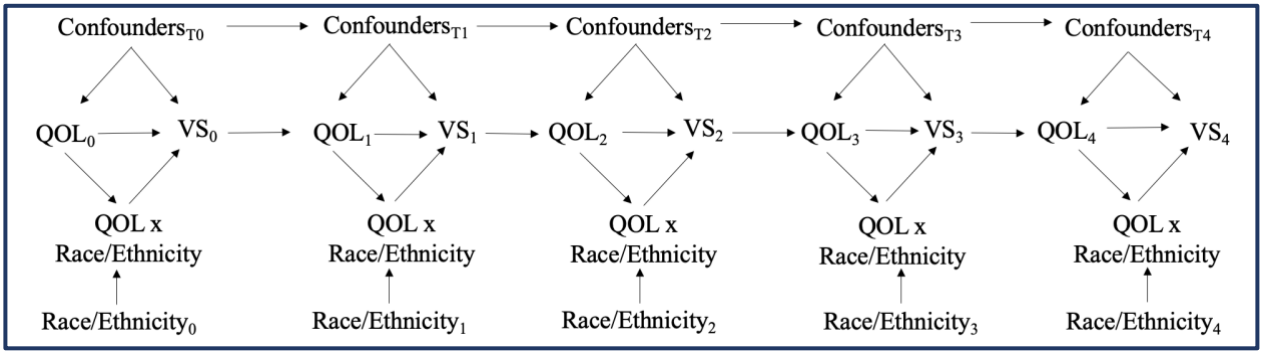


Figure 4.3. Average number of women living with HIV in the cohort who are virally suppressed at each time point.

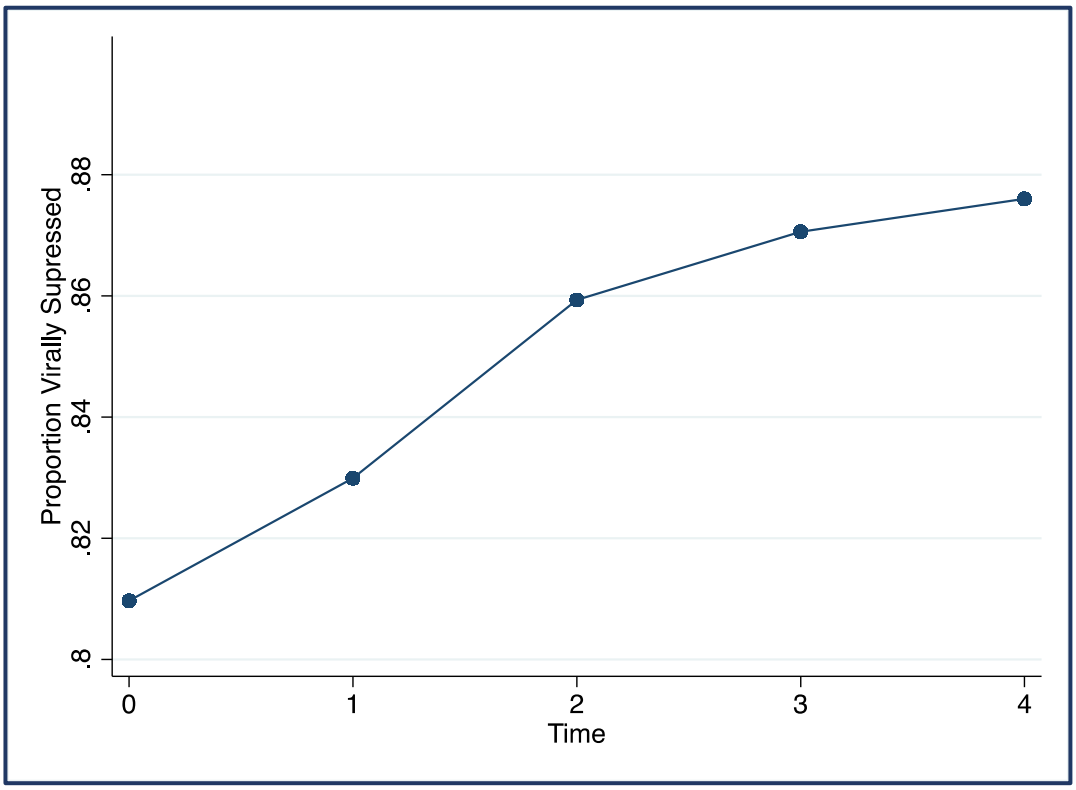
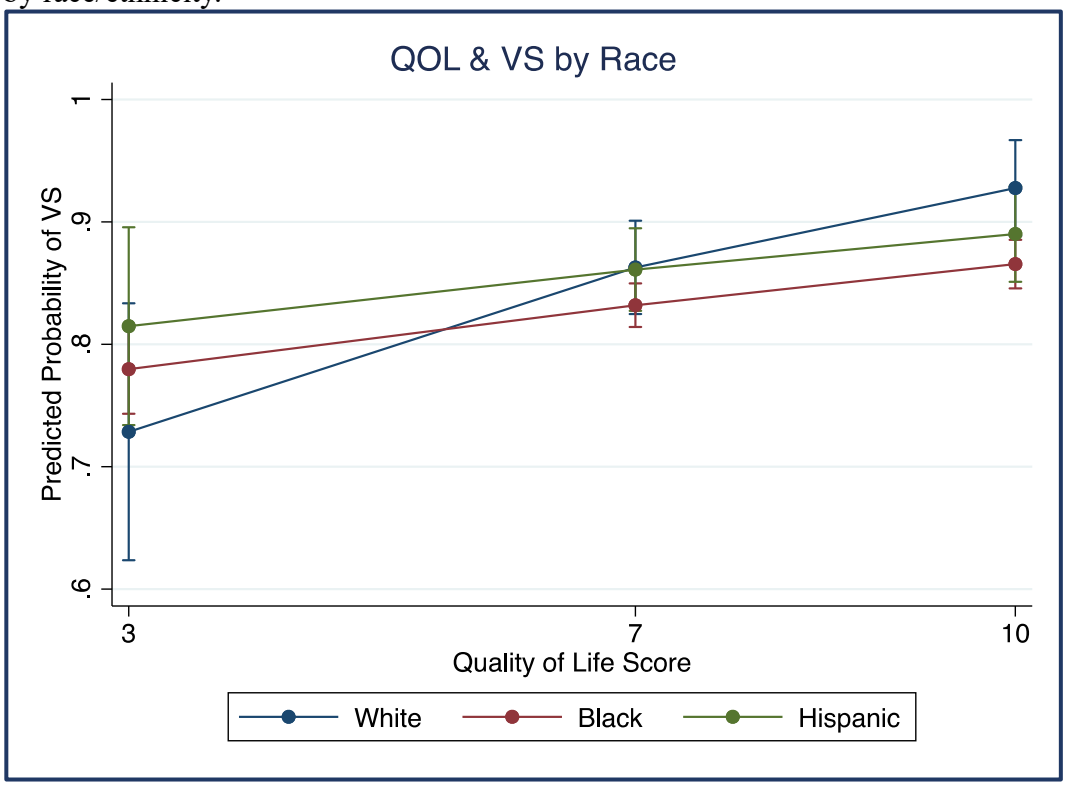


Figure 4.4. Predicted probabilities of viral suppression at various quality of life by race/ethnicity.



Chapter 5

Dissertation Conclusion

This dissertation presents an investigation into the specific impacts of neighborhood socio-environmental factors, individual health experiences, and self-assessed quality of life on viral suppression among PLWH. Conducted across distinct geographic locations and populations, our research was structured around three specific aims, each examining these factors independently to understand their unique contributions to health outcomes in the context of HIV.

Our first aim addressed the role of neighborhood characteristics, such as walkability, transportation options, and socio-economic status, in influencing viral suppression. We found that areas with poor infrastructure and lower socio-economic conditions are linked to lower rates of viral suppression. This underscores the importance of environmental and economic support in enhancing access to healthcare and adherence to HIV treatment regimes. Effective interventions must, therefore, target these neighborhood disparities to improve health outcomes for PLWH.

The second aim delved into how individual health experiences, specifically pain perception, impact viral suppression. Contrary to expectations, our findings indicated that experiencing moderate to severe pain did not significantly detract from the likelihood of achieving viral suppression. This suggests that despite the challenges pain can pose, it may not directly compromise the efficacy of ART adherence among women in our study. However, this could differ in broader populations, for example among populations who report stimulant use, therefore further research is necessary to explore these dynamics.

Lastly, our third aim explored the influence of self-reported quality of life on viral suppression. The results demonstrate a positive correlation: as perceived quality of life improves, so does the likelihood of viral suppression. This relationship held true across all demographic

groups, although the degree of impact varied by race and ethnicity, highlighting potential areas for culturally tailored interventions.

By examining these factors independently, this research contributes nuanced insights into the diverse elements that affect health outcomes in PLWH. Each factor—environmental, personal health, and quality of life—plays a crucial role, and understanding their individual impacts allows for the development of targeted, effective interventions. These findings not only advance our knowledge of HIV management but also emphasize the need for a multi-faceted approach that addresses the specific needs and circumstances of individuals living with HIV. Such strategies are essential for improving not just health outcomes but also the overall wellbeing of PLWH.

Supplemental Tables

Table S1. Frequency and percentage of missing values in the variables of interest for study 2.

Variables	Number (%) Missing
Viral Suppression	15 (1.05)
Pain	11 (0.77)
Medication Use	7 (0.49)
Substance Use	6 (0.42)
Income	30 (2.10)
Education	1 (0.07)
Age at Visit	0 (0)
STI	2 (0.14)
Race/Ethnicity	0 (0)
Depression	12 (0.84)
Heavy Alcohol Consumption	5 (0.35)
Sexual Identity	3 (0.21)
Employment	1 (0.07)
Insurance Coverage	7 (0.49)
Current Cigarette Use	0 (0)
Marijuana Use	6 (0.42)

Table S2. Estimated odds ratios (ORs) with 95% CI for the analysis of the association between viral suppression and pain.

Characteristics	Model A:		Model B:		Model C:	
	aOR	(95% CI)	aOR	(95% CI)	aOR	(95% CI)
Pain	1.05	(0.75, 1.47)	1.01	(0.69, 1.45)	1.02	(0.70, 1.48)
Age at Visit	**1.04*****	**(1.02, 1.06)**	**1.05*****	**(1.03, 1.07)**	**1.05*****	**(1.03, 1.07)**
Income (<200% FPL)	0.98	(0.64, 1.50)	1.08	(0.69, 1.70)	1.04	(0.64, 1.60)
Education						
< High School (HS)	-	-	-	-	-	-
HS/Equivalent	1.17	(0.79, 1.75)	1.23	(0.81, 1.87)	1.11	(0.72, 1.70)
Advanced Degree	1.02	(0.69, 1.52)	0.95	(0.63, 1.44)	0.85	(0.56, 1.30)
Employment	1.42*	(0.96, 2.08)	1.26	(0.84, 1.89)	1.17	(0.77, 1.78)
Race/Ethnicity						
White	-	-	-	-	-	-
Black	0.82	(0.64, 1.43)	0.77	(0.42, 1.39)	0.84	(0.46, 1.53)
Hispanic/Latinx	1.02	(0.51, 2.08)	1.11	(0.53, 2.32)	1.10	(0.52, 2.31)
Asian/HPI/NA/AN/Other	0.73	(0.26, 2.04)	0.87	(0.29, 2.60)	0.82	(0.27, 2.48)
Depression			0.75	(0.52, 1.08)	0.85	(0.58, 1.25)
Years Living with HIV			**0.96****	**(0.94, 0.99)**	**0.96****	**(0.94, 0.99)**
Hospitalized			0.86	(0.58, 1.27)	0.86	(0.57, 1.28)
Cancer History			1.16	(0.57, 2.36)	1.10	(0.53, 2.26)
STI			0.75	(0.38, 1.47)	1.01	(0.49, 2.08)
Pain Medication Use			1.41*	(0.95, 2.10)	1.48*	(0.99, 2.23)
Cannabis Use					0.79	(0.51, 1.22)
Heavy Alcohol Consumption					**0.58****	**(0.36, 0.95)**
Stimulant Use					**0.36*****	**(0.20, 0.66)**
Cigarette Use					0.78	(0.54, 1.14)
Other Substances					1.10	(0.39, 3.05)

$^{*}0.05 \leq p < 0.1$; $^{**}0.001 \leq p < 0.05$ (bold font); $^{***}p < 0.001$ (bold font). Model A controls for demographic and socioeconomic variables. Model B controls for all the variables in Model A as well as variables related to health status and pain medication use. Model C includes all prior variables in Models A & B as well as substance use variables.

Table S3. Frequency and percentage of missing values in the variables of interest at Time 0 for study 3.

Variables	Number (%) Missing
Viral Suppression	17 (1.26)
Quality of Life	18 (1.34)
Pain	21 (1.56)
Substance Use	30 (0.41)
Income	270 (3.68)
Education	5 (0.07)
Age at Visit	0 (0)
STI	20 (0.27)
Race/Ethnicity	0 (0)
Depression	72 (0.98)
Heavy Alcohol Consumption	30 (0.41)
Sexual Identity	15 (0.20)
Employment	7 (0.10)
Insurance Coverage	34 (0.46)
Current Cigarette Use	0 (0)
Marijuana Use	32 (0.44)

Table S4. Estimated odds ratios (ORs) with 95% CI for the analysis of the association between viral suppression and quality of life.

Characteristics	Model A:		Model B:		Model C:	
	aOR	(95% CI)	aOR	(95% CI)	aOR	(95% CI)
Quality of Life Score	**1.2*****	**(1.13, 1.28)**	**1.18*****	**(1.10, 1.26)**	**1.17****	**(1.10, 1.25)**
Age at First Visit	**1.07*****	**(1.05, 1.11)**	**1.08*****	**(1.05, 1.10)**	**1.08*****	**(1.05, 1.10)**
Income (<200% FPL)	1.06	(0.78, 1.43)	1.05	(0.77, 1.43)	1.03	(0.76, 1.40)
Education						
< High School (HS)	-	-	-	-	-	-
HS/Equivalent	1.41*	(0.94, 2.10)	1.38	(0.92, 1.06)	1.29	(0.87, 1.92)
Advanced Degree	**1.59****	**(1.06, 2.38)**	**1.54****	**(1.03, 2.31)**	1.43*	(0.95, 2.15)
Time						
Zero (Visit 40)	-	-	-	-	-	-
One (Visit 42)	**1.34****	**(1.02, 1.77)**	**1.35****	**(1.03, 1.78)**	**1.36****	**(1.03, 1.79)**
Two (Visit 44)	**1.78*****	**(1.34, 2.37)**	**1.79*****	**(1.34, 2.38)**	**1.81*****	**(1.36, 2.40)**
Three (Visit 46)	**2.21*****	**(1.64, 2.98)**	**2.19*****	**(1.62, 2.95)**	**2.18*****	**(1.61. 2.94)**
Four (Visit 48)	**2.21*****	**(1.63, 2.99)**	**2.24*****	**(1.65, 3.03)**	**2.28*****	**(1.68, 3.10)**
Race & Ethnicity						
White	-	-	-	-	-	-
Black	0.71	(0.39, 1.24)	0.68	(0.38, 1.21)	0.62	(0.37, 1.17)
Hispanic/Latinx	1.15	(0.56, 2.34)	1.13	(0.55, 2.30)	1.00	(0.49, 2.04)
Asian/HPI/NA/AN/Other	0.83	(0.29, 2.39)	0.79	(0.27, 2.27)	0.77	(0.26, 2.21)
Depression			**0.76****	**(0.58, 0.99)**	0.84	(0.64, 1.09)
Years Living with HIV			0.99	(0.96, 1.02)	0.99	(0.96, 1.01)
Cancer History					1.08	(0.55, 2.14)
Illegal Substance Use[§]					**0.47*****	**(0.35, 0.63)**
Heavy Drinking					0.72*	(0.50, 1.04)

$^{*}0.05 \leq p < 0.1$; $^{**}0.001 \leq p < 0.05$ (bold font); $^{***}p < 0.001$ (bold font). Model A controls for time, demographic, and socioeconomic variables. Model B controls for all the variables in Model A as well as variables related to health status and health behaviors. Model C includes all prior variables in Models A & B as well as an interaction term between race/ethnicity and quality of life score. [§] Illegal substance use includes cocaine, crack, heroin, methamphetamines, amphetamines, injection drugs, non-injected recreational drugs, use of prescription drugs in a way not as prescribed, tranquilizers.

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