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Examining the Effects of Individual and Neighborhood Factors on HIV Transmission Risk Potential among People With HIV

Semiu Olatunde Gbadamosi
sgbad002@fiu.edu

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FLORIDA INTERNATIONAL UNIVERSITY

Miami, Florida

EXAMINING THE EFFECTS OF INDIVIDUAL AND NEIGHBORHOOD FACTORS ON HIV TRANSMISSION RISK POTENTIAL AMONG PEOPLE WITH HIV

A dissertation submitted in partial fulfillment of

the requirements for the degree of

DOCTOR OF PHILOSOPHY

in

PUBLIC HEALTH

by

Semiu Olatunde Gbadamosi

2022

To: Dean Tomás R. Guilarte
Robert Stempel College of Public Health and Social Work

This dissertation, written by Semiu Olatunde Gbadamosi, and entitled Examining the Effects of Individual and Neighborhood Factors on HIV Transmission Risk Potential among People with HIV, having been approved in respect to style and intellectual content, is referred to you for judgment.

We have read this dissertation and recommend that it be approved.

Mary Jo Trepka

Zoran Bursac

Andrea Raymond

Diana M. Sheehan, Major Professor

Date of Defense: March 28, 2022

The dissertation of Semiu Olatunde Gbadamosi is approved.

Dean Tomás R. Guilarte
Robert Stempel College of Public Health and Social Work

Andrés G. Gil
Vice President for Research and Economic Development
and Dean of the University Graduate School

Florida International University, 2022

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DEDICATION

This dissertation is dedicated to my wife, Funke; daughter, Ari; and son, Fi: your love and support got me through this academic journey. I will be eternally indebted to you for your patience and understanding. It is time to celebrate; you earned this degree right along with me. And to my late parents, I am forever grateful to them for setting me off on the road to success.

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ABSTRACT OF THE DISSERTATION

EXAMINING THE EFFECTS OF INDIVIDUAL AND NEIGHBORHOOD FACTORS ON HIV TRANSMISSION RISK POTENTIAL AMONG PEOPLE WITH HIV

by

Semiu Olatunde Gbadamosi

Florida International University, 2022

Miami, Florida

Professor Diana M. Sheehan, Major Professor

HIV transmission risk significantly increases in late-diagnosed HIV and at HIV viral load (VL) >1500 copies/mL. The objective of this dissertation was to examine factors associated with HIV transmission risk potential for persons with HIV (PWH) using measures of time from HIV infection to diagnosis and trajectories of VL suppression. Additionally, we sought to determine whether a single yearly VL measure—the current standard to track the HIV epidemic in the United States—is reliable in assessing viral suppression for PWH.

The first study estimated the distribution of time from HIV infection to diagnosis in Florida using a CD4 depletion model and utilized a frailty model to determine individual- and neighborhood-level factors associated with receiving a diagnosis within 40 months after HIV infection (based on the most recent median time from HIV infection to diagnosis in 2018 reported in a U.S. national study). Overall, the median time to diagnosis was 83 months and was stable during 2014-2018. Older adults, non-Hispanic Blacks (vs. non-Hispanic Whites), and heterosexual males (vs. men who have sex with men) were less likely to be diagnosed within 40 months after HIV infection. The second study examined agreement between three viral suppression measures among clients in the Miami-Dade County Ryan White Program (RWP): recent viral suppression, defined

as having a suppressed VL (<200 copies/mL) in the last test in 2017; maintained viral suppression, having a suppressed VL for both the first and last VL tests in 2017; and sustained viral suppression, having all VL tests in 2017 showing suppression. Recent viral suppression measures overestimated maintained and sustained viral suppression measures by 7.0% and 10.1%, respectively. Non-Hispanic Blacks (0.88 [0.74-1.00]) and Haitians (0.87 [0.72-1.00]) had lower Gwet's agreement coefficient scores than Hispanics (0.94 [0.87-1.00]) and non-Hispanic Whites/Others (0.93 [0.82-1.00]) across all three definitions. The third study determined the percentage of person-time spent with VL >1500 copies/mL and utilized a random-effects zero-inflated negative binomial model to determine factors associated with experiencing longer time with VL >1500 copies/mL for 6390 RWP clients. On average, clients spent 27.4 days per year at substantial risk of transmitting HIV. Younger age, AIDS diagnosis, and drug use in the preceding 12 months were associated with longer time spent at VL >1500 copies/mL.

In conclusion, a substantial number of individuals lived with HIV for a long time before their diagnosis in Florida, and on average, PWH spent nearly a month per year at substantial risk of transmitting HIV. Policies and tailored interventions targeting the specific HIV needs of underserved populations may help reduce transmission risk. Reporting viral suppression estimates using maintained or sustained viral suppression in addition to recent viral suppression may be beneficial in clinical care and for adequate monitoring of programmatic outcomes.

TABLE OF CONTENTS

ABBREVIATIONS AND ACRONYMS

-2LL	Likelihood Value Statistics
ACA	Affordable Care Act
ACS	American Community Survey
AC1	Gwet's Agreement Coefficient
AIC	Akaike Information Criteria
AICC	Corrected Akaike Information Criteria
AHR	Adjusted Hazard Ratio
AOR	Adjusted Odds Ratio
ARR	Adjusted Rate Ratio
ART	Antiretroviral Therapy
BIC	Bayesian Information Criteria
CD4	Cluster of Differentiation 4
CDC	Centers for Disease Control and Prevention
CI	Confidence Intervals
EAPC	Estimated Annual Percent Change
eHARS	Enhanced HIV/AIDS Reporting System
EHE	Ending the HIV Epidemic
FPL	Federal Poverty Level
HR	Hazard Ratio
IDU	Injection Drug Use
IQR	Interquartile Range
MSM	Men who Have Sex with Men
NB	Negative Binomial

NPV	Negative Predictive Value
PPV	Positive Predictive Value
PWH	People with HIV
RUCA	Rural-Urban Community Area Codes
RWP	Ryan White HIV/AIDS Program
U.S.	United States
ZCTA	ZIP Code Tabulation Areas
ZIP	Zone Improvement Plan
ZIP	Zero-Inflated Poisson
ZINB	Zero-Inflated Negative Binomial

INTRODUCTION

Substantial gaps remain in the response to the HIV epidemic in the state of Florida. In 2019, the estimated HIV prevalence (701.3 per 100,000) in Florida was 1.6 times the United States (U.S.) national estimate, and an estimated 13.5% of these persons with HIV (PWH) in the state were undiagnosed (Centers for Disease Control and Prevention, 2021). Approximately 13.5% of the newly diagnosed HIV infections in the U.S. in 2019 were in Florida, representing the highest number of HIV diagnoses across states in the U.S (Centers for Disease Control and Prevention, 2020). Of the 4,334 persons diagnosed with HIV in Florida in 2019, about 80.0% were racial/ethnic minorities, with African Americans accounting for 62.0%, and Hispanic/Latinos representing 33.5% of new diagnoses (Centers for Disease Control and Prevention, 2019). Additionally, 33% of the diagnosed PWH in Florida in 2019 were not virally suppressed (Centers for Disease Control and Prevention, 2019). One of the goals of the U.S. National HIV/AIDS Strategy is to reduce the number of new diagnoses by at least 25 percent (The White House, 2021). To effectively reduce the number of new infections, secondary HIV prevention strategies focused on reducing HIV transmission risk potential among PWH are needed.

Early identification of undiagnosed PWH remains a critical component to prevent transmission of HIV. Early HIV diagnosis and engagement with HIV care services have shown remarkable results such that a person with HIV that is diagnosed and linked to HIV care early is more likely to be virally suppressed (Hall et al., 2013), less likely to transmit the virus to an uninfected (Marks et al., 2005), and have better health outcomes (Palella et al., 2003) than those with a late diagnosis. In an analysis of 2018 data from the Behavioral Risk Factor Surveillance System, among Florida residents aged 18 years or older, only about 45% of people surveyed reported ever been tested for HIV (Centers

for Disease Control and Prevention et al., 2015), suggesting HIV testing rates are low in the state and fall short of current national targets (The White House, 2021); resulting in a high prevalence of late diagnosis (Trepka et al., 2014). The window for effective interventions during the acute phase of infection is reduced with late diagnosis, increasing the risk of transmission. In rural Florida, older age and male sex were linked to late diagnosis (Trepka et al., 2014). Whereas in urban areas, Hispanic and non-Hispanic black race/ethnicity, nativity, and heterosexual mode of transmission were determinants of late diagnosis (Trepka et al., 2014). Concerns about stigma (Murray et al., 2017), low perceived personal risk (Cianelli et al., 2019; Lopez-Quintero et al., 2016), and inaccessibility to HIV testing sites have been reported as impeding optimal HIV testing uptake in the population (Murray et al., 2017; Sutton et al., 2010).

The goal to accelerate the decline in new HIV infections is unlikely to be achieved without a significant reduction in the time from HIV infection to diagnosis. Time from infection to HIV diagnosis provides information on whether HIV testing initiatives capture early or late HIV diagnosis of PWH. However, given the difficulty in ascertaining the specific time point that an individual is infected with the virus, the time interval from HIV infection to diagnosis is not readily measured. Modeling studies estimating median time from HIV infection to diagnosis in the U.S. have reported a 5-year time length between infection and diagnosis in the early 2000s (Hall et al., 2015). More recently, and following concerted efforts to improve routine HIV testing, population estimates of 3 years have been reported (Dailey et al., 2017) suggesting a downward trend in the number of years infected at the time of HIV diagnosis for newly diagnosed PWH. Research has also shown that the time a PWH remains undiagnosed represents one of the periods of highest transmission risk potential to an uninfected partner (Hall et al., 2012; Ratmann et al., 2016). Moreover, a study found that approximately 49% of

transmissions were attributed to the 20% of PWH who are undiagnosed (Hall et al., 2012). Although several national studies (Crepaz et al., 2021; Dailey et al., 2017; Hall et al., 2015; Peruski et al., 2021) have been conducted in the U.S. to estimate the time from infection to HIV diagnosis, no study has reported on whether racial/ethnic disparities exist for the state of Florida. Understanding the population-level distribution of time from infection to HIV diagnosis may be beneficial in public health monitoring and targeted outreach activities to increase routine HIV testing in populations at risk.

PWH who are aware of their infection and poorly retained in care contribute disproportionately to the overall transmission of HIV. Although this group represents 45% of the total population of PWH, they contribute 61% of transmissions (Skarbinski et al., 2015). For this group, consistent retention in care and achieving viral suppression would confer therapeutic and preventive benefits leading to significant reductions in HIV transmission (Bavinton et al., 2018; Cohen et al., 2016; Rodger et al., 2016).

Currently, recipients of the Ryan White HIV/AIDS Program funding utilize a noncumulative quantitative assessment of HIV viral load suppression defined as having "<200 copies/ml at last HIV viral load test during the measurement year" to monitor programmatic outcomes (Department of Health and Human Services, 2019). In addition, the single yearly viral load measure is the current standard of viral suppression definition used to monitor the HIV epidemic in the U.S. While the last viral load has demonstrated clinical value in determining treatment efficacy and the prognosis of PWH receiving care (Marschner et al., 1998; Murray et al., 1999), the utility of this measure in assessing a patient's viral load dynamics over time is limited. Recently, some authors have argued that longitudinal cumulative measures of viral load such as maintained and sustained viral suppression (Crepaz et al., 2018; Marks et al., 2016), and person-time spent with viral load >1500 copies/mL (Crepaz et al., 2018; Lesko et al., 2018; Marks et al., 2015)

may be more beneficial in estimating transmission risk potential given the fluctuations in viral load expected over time. One study found that a single viral load measure may overestimate sustained viral suppression by 16% (Marks et al., 2016). Sustained HIV viral suppression in PWH in care reduces HIV transmission rate to uninfected persons to as low as 0 per 100 person-years (Li et al., 2019). Experiencing longer time with viral load >1,500 copies/mL exacerbates the risk for HIV transmission among PWH (Quinn et al., 2000). A recent study found that the average time spent with viral load >1,500 copies/mL for PWH aged 13-29 years was 206 days suggesting that this population had a high risk of transmitting HIV for more than half of the year (Crepaz et al., 2020). Relative to Hispanics and Whites, Blacks experienced a longer percentage of time during 2014 with viral load >1,500 copies/mL suggesting racial disparities in HIV transmission potential (Lesko et al., 2018). No study has reported on whether racial/ethnic disparities or age differences in person-time spent with viral load >1500 copies/mL exist for Florida.

Although individual-level risk factors are major drivers of HIV transmission, these factors often do not occur in isolation. For example, evidence of variations in risk behavior among racial/ethnic groups do not fully describe the relationship between racial/ethnic disparities and HIV incidence (Hallfors et al., 2007; Tillerson, 2008). Increasingly, researchers are recognizing the importance of studying the impact of neighborhood contextual factors on the population-level risk for HIV transmission (Bowleg et al., 2014; Brawner et al., 2017; Chandran et al., 2019). Factors such as neighborhood poverty (Wiewel et al., 2016), social disorder (Latkin et al., 2007), structural violence (Latkin et al., 2005, 2007), and economic deprivation (Zierler et al., 2000) as determinants of risk behavior may explain a significant degree of the disparities in HIV transmission. Understanding the interdependence of these contextual factors with

race/ethnicity is key to developing and implementing effective secondary prevention strategies to reduce transmission risk, particularly in minority populations.

Research Objective

The objective of this dissertation was to examine factors associated with HIV transmission risk potential for PWH using measures of time from HIV infection to diagnosis and trajectories of viral load suppression. Additionally, this dissertation sought to determine whether a single yearly viral load measure—the current standard to track the HIV epidemic in the United States—is reliable in assessing viral suppression for PWH.

Study aims and hypotheses

Aim 1: To estimate the distribution of time from HIV infection to diagnosis and assess the individual- and neighborhood-level factors associated with the length of time from HIV infection to diagnosis for PWH in Florida.

Hypothesis 1a: Longer median time between HIV infection and diagnosis will be observed among racial/ethnic minorities compared with non-Hispanic Whites.

Hypothesis 1b: Older adults will have longer median time from HIV infection to diagnosis than younger adults.

Hypothesis 1c: Residing in a neighborhood with worse socioeconomic factors will be associated with longer median time from HIV infection to diagnosis.

Aim 2: To examine how different definitions of viral suppression characterize PWH in the RWP and quantify the degree of agreement between viral suppression definitions.

Hypothesis 2: Single viral load measure will overestimate maintained and sustained viral suppression by a greater degree for racial/ethnic minorities than for non-Hispanic Whites.

Aim 3: To determine the percentage of person-time spent with viral load above 1500 copies/mL and the associations of demographic, clinical, and psychosocial factors, and this outcome among persons with HIV receiving care in Miami-Dade County.

Hypothesis 3a: Racial/ethnic minorities will spend longer time with viral load >1500 copies/mL than non-Hispanic Whites.

Hypothesis 3b: Younger adults will spend longer time with viral load >1500 copies/mL than older adults.

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MANUSCRIPT 1

Time from HIV Infection to Diagnosis in Florida, 2014-2018: The Role of Individual and Neighborhood Factors

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Abstract

Understanding the factors that influence the length of time from HIV infection to diagnosis is critical to minimizing HIV transmission events. The study's objective was to estimate the distribution of time from HIV infection to diagnosis and assess the individual- and neighborhood-level factors associated with the length of time from HIV infection to diagnosis for PWH in Florida. Using Florida's HIV surveillance data linked with 2013–2017 American Community Survey data by residential ZIP code, we examined a cohort of individuals ≥ 13 years diagnosed with HIV in Florida during 2014-2018. We estimated the median time from HIV infection to diagnosis, overall, and by year of diagnosis stratifying by individual- and neighborhood-level characteristics. A frailty model was used to evaluate the association between receiving a diagnosis within 40 months after HIV infection (based on the median time from HIV infection to diagnosis in a U.S. national study) and covariates. Among 11,566 individuals (79% male, 45% non-Hispanic Black, 56% men who have sex with men [MSM], and 98.3% urban residents), the median time from HIV infection to diagnosis was 83 months (interquartile range: 42.0, 150.0). The median time was stable during 2014–2018 (estimated annual percent change -2.4% [95% CI: -8.8, 4.5]). Overall, 23.8% of PWH were diagnosed within 40 months of HIV infection. Lower percentages of individuals aged 55+ years (17.0%), females (23.0%), non-Hispanic Blacks (22.2% vs. non-Hispanic Whites [26.2%]), and heterosexual males (19.1% vs. MSM [25.2%]) were diagnosed within 40 months. Minimal variation was observed across neighborhood-level variables (22.2% to

25.9%). In multivariable analysis, older adults, non-Hispanic Blacks, or heterosexual males were less likely to be diagnosed with HIV within 40 months. One-half of individuals diagnosed with HIV in Florida during 2014-2018 lived with HIV for 83 months or more before diagnosis. The median time remained stable over the years. Tailored HIV testing initiatives targeting older adults, non-Hispanic Blacks and heterosexual males may provide opportunities for early care and subsequent reduction in onward HIV transmission.

Introduction

Early identification of undiagnosed persons with HIV (PWH) remains a critical component in preventing HIV transmission in line with the United States (U.S.) Ending the HIV Epidemic (EHE) initiative and the National HIV/AIDS Strategy (Fauci et al., 2019; The White House, 2021). In 2019, approximately 34,000 individuals were newly diagnosed with HIV in the U.S., and an estimated 20.2% were diagnosed late (defined as having AIDS at initial HIV diagnosis) (Centers for Disease Control and Prevention, 2019a). Early HIV diagnosis provides opportunities for early antiretroviral therapy (ART) initiation (Hall et al., 2013), allows for the adoption of risk-reduction behaviors (Marks et al., 2005), and decreases risks of morbidity and mortality and transmitting HIV (Palella et al., 2003). Whereas in late-diagnosed infection, the window of opportunity for effective interventions during the acute phase of infection is minimized, and this has significant implications for onward HIV transmission. For example, a Centers for Disease and Prevention Control (CDC) study found that the highest transmission rates were in PWH who were undiagnosed and in the early stage of infection (Li et al., 2019). To accelerate the decline in new HIV infections, HIV testing initiatives focused on early detection of HIV and early access to ART may achieve the most significant impact.

Measuring the length of time from HIV infection to diagnosis is critical in monitoring and assessing the performance of HIV testing initiatives and their impact on capturing early or late disease states. However, the uncertainty about the specific time of HIV exposure makes it practically impossible to accurately determine the time of infection, particularly for people who do not have a regular history of testing. A recent systematic review found that the back-calculation approach and the CD4 depletion model were commonly used in estimating the duration of HIV infection at the time of diagnosis (Gbadamosi et al., 2021). While the back-calculation method requires the specification of the AIDS incubation distribution, which is often unreliable given advancements in HIV treatment and fewer AIDS diagnoses, the CD4 depletion model uses individual-level CD4 data at the time of diagnosis to estimate this measure. The review also reported that the average length of time from HIV infection to diagnosis in high- and middle-income countries was 3 years from 1996 to 2015 (Gbadamosi et al., 2021). In the U.S., studies using the CD4 depletion model have estimated a median time of 36 to 60 months in the early 2000s (Hall et al., 2015; Robertson et al., 2020) and more recently, 40 to 43 months in 2018 (Crepaz et al., 2021; Peruski et al., 2021), following concerted efforts to improve routine HIV testing (Branson et al., 2006; Centers for Disease Control and Prevention, 2013, 2019c, 2019d).

According to the CDC, every individual aged 13 to 64 should get tested for HIV at least once in their lifetime, and at-risk populations may benefit from more frequent testing at least annually (Branson et al., 2006). In 2018, only about half of the Behavioral Risk Factor Surveillance System (BRFSS) survey respondents aged 18 years and older in Florida had ever been tested for HIV (Centers for Disease Control and Prevention et al., 2015), which is suboptimal. In 2019, an estimated 20.9% of newly diagnosed PWH in Florida were diagnosed late (Centers for Disease Control and Prevention, 2019a).

Previous studies have shown that individual-level factors such as concerns about stigma, (Murray et al., 2017) low perceived personal risk (Cianelli et al., 2019; Lopez-Quintero et al., 2016), and inaccessibility to HIV testing locations (Murray et al., 2017; Sutton et al., 2010) may act as barriers to HIV testing uptake, which may inadvertently lead to delays in diagnoses.

Although individual-level factors are significant drivers of HIV outcomes, they often do not occur in isolation. An extensive body of work demonstrates where people also reside matters when assessing HIV-related outcomes (Burke-Miller et al., 2016; Dawit et al., 2021; Mukolo et al., 2013; Olatosi et al., 2020; Ransome et al., 2016; Trepka et al., 2020). Additionally, some PWH may experience health disparities depending on residence in a particular neighborhood (Biello et al., 2013; Dawit et al., 2021). For example, evidence of variations in risk behavior among racial/ethnic groups does not fully describe the relationship between racial/ethnic disparities and HIV incidence (Hallfors et al., 2007; Tillerson, 2008). Factors such as neighborhood poverty (Wiewel et al., 2016), social disorder (Latkin et al., 2007), structural violence (Latkin et al., 2005, 2007), and economic deprivation (Zierler et al., 2000) as determinants of risk behavior may explain a significant degree of the disparities in HIV transmission risk. In New York City, neighborhood socioeconomic deprivation was associated with late diagnosis (Ransome et al., 2016). In rural areas in Florida, older age and male sex were associated with late diagnosis (Trepka et al., 2014). Whereas in urban areas, racial/ethnic disparities exist with Hispanics and non-Hispanic Blacks more likely to be diagnosed late compared with non-Hispanic Whites (Trepka et al., 2014). Yet, little is known about the impact of neighborhood-level factors on the length of time from HIV infection to diagnosis. Therefore, the objective of this study was to estimate the distribution of time from HIV infection to diagnosis and assess the individual- and

neighborhood-level factors associated with the length of time from HIV infection to diagnosis for PWH in Florida.

Methods

We used data from the Florida Department of Health's enhanced HIV/AIDS Reporting System (eHARS) for 2014 to 2018 with records on individuals diagnosed with HIV and residing in Florida for this retrospective analysis. The eHARS contains individual-level demographic and laboratory data, including HIV diagnosis based on the CDC's revised HIV surveillance case definition (Centers for Disease Control and Prevention, 2014). Five-year estimates of zone improvement plan (ZIP) code tabulation area (ZCTA)-level (neighborhood) socioeconomic data from the 2013–2017 American Community Survey (ACS) (U.S. Census Bureau, 2018) were also obtained. Individuals aged 13 years and older diagnosed during 2015-2018 were included (N=25,284). Cases with invalid or missing CD4 count at diagnosis (n=2,644), missing first viral load (n=3854), missing or invalid data for ZIP code (n=125) or diagnosis in a correctional facility (n=500) or perinatally infected (n=29) were excluded from this study.

Individual- and neighborhood-level variables

Individual-level variables extracted from the eHARS dataset included age at diagnosis, sex at birth, race, ethnicity, HIV transmission category, HIV diagnosis date, first CD4 test, first CD4 test date, first detectable viral load measurement, and residential ZIP code at the time of HIV diagnosis. In addition, four neighborhood-level socioeconomic variables were extracted from the ACS: the percent of the population aged ≥16 who were unemployed; the percent of the population aged ≥25 with less than a 12th-grade education; the percent of households living in rented housing, and the percent of households with annual income <$15,000. These variables were represented as 'high unemployment,' 'low education,' 'high rented housing,' and 'low household

income,' respectively and categorized based on their quartiles from the 1st (lowest) to the 4th quartile (highest). To determine the rural/urban status of neighborhoods, we used the ZIP code-based data of the Rural-Urban Commuting Area Codes (RUCA) developed by the University of Washington WWAMI Rural Research Center (WWAMI Rural Health Research Center, n.d.). Individual- and neighborhood-level data were merged by matching each individual's ZIP code at the time of HIV diagnosis with the ZIP code's corresponding ZCTA.

Time from HIV infection to diagnosis

We used the first CD4 test after HIV diagnosis to model the CD4 depletion trajectory (Model 1) and estimated the time from HIV infection to diagnosis, T_i, for each individual in the study (Model 2), as described in the literature (Dailey et al., 2017; Lodi et al., 2011; Song et al., 2017a).

Model 1: $\sqrt{CD4(t)} = a_i + (b_i \times t) + e_{it}$

Model 2: $T_i = \frac{\sqrt{firstCD4} - a_i}{b_i}$

Briefly, parameters for the intercept and slope, a_i and b_i, stratified by age group, sex, and transmission risk category, were obtained from published estimates in previous studies (Lodi et al., 2011; Song et al., 2017a). To ensure comparability with national studies, we applied the published estimates for individuals in the 15-19 age group to those aged 13-19 in our study. We restricted our analysis to individuals with at least one CD4 count measured before ART initiation. Individuals with evidence of ART use such as CD4 count >500 and viral load measurement <200 copies/mL were excluded. Because the age at HIV infection was unknown, we first estimated T_i using the age group at diagnosis as the CD4 depletion modeling age group. Then, we estimated the age at HIV infection by subtracting T_i from the age at diagnosis. We also calculated the

date of infection for each individual by subtracting T_i from the date of diagnosis. We encountered model artifacts that led to negative values of T_i, which corresponded to an infection date after the date of diagnosis. In this situation, we reset the date of infection to be the same as the date of diagnosis as in previous studies (Robertson et al., 2020; Song et al., 2017b). For individuals with an estimated age at HIV infection below 13 years, we reset the date of infection to the date they reached age 13 to be consistent with our study population definition. We then reran the CD4 depletion model using the new estimated age at HIV infection to compute T_i. Finally, to account for the rapid temporary decline in CD4 count during the acute phase of HIV infection (Langford et al., 2007; Okoye & Picker, 2013), we restricted the remainder of our analysis to individuals with $T_i > 2$ months.

Analytical plan

Descriptive statistics, including frequency and percentage distributions, were used to describe the study population during 2014–2018**.** The median and interquartile range (IQR) of time from HIV infection to diagnosis for the population overall and by year of diagnosis were calculated and stratified by individual- and neighborhood-level characteristics. Using Poisson regression analysis with a log link function, we examined temporal trends over time. The estimated annual percentage change (EAPC), a summary measure to describe the average year-to-year change in the median time from HIV infection to diagnosis from 2014 to 2018, and the 95% confidence intervals (CI) were computed. Further, we calculated the proportion of individuals who received a diagnosis within 40 months after HIV infection by individual- and neighborhood-level characteristics. We selected this cut-off (40 months) based on the most recent median time from HIV infection to diagnosis in 2018 reported in a CDC study (Crepaz et al., 2021). Individuals who did not receive an HIV diagnosis within this cut-off timepoint were

right-censored. Hazard ratios (HR) and 95% CI from univariable Cox proportional hazards regression models were calculated to assess the association between receiving a diagnosis within 40 months after HIV infection and each covariate. We presumed that individuals who share similar characteristics tend to cluster within the same neighborhood, and thus measurements on individuals who reside in the same neighborhood may be correlated. For this reason, we fitted a multivariable model and included a frailty term (random effects). The frailty term accounted for the within-cluster homogeneity induced by unobserved neighborhood characteristics and was modeled using a log-normal distribution. All covariates were included in the frailty model. We also fitted the models testing the gamma distribution assumption.

All statistical tests were conducted using SAS/STATv14.2 (SAS Institute Inc, 2016). All P-values reported were two-sided, and P <.05 was considered statistically significant. This study was approved by the institutional review boards at Florida International University, Miami, and the Florida Department of Health.

Results

The analytic cohort included 11,566 individuals diagnosed with HIV during 2014–2018 residing in 789 unique ZCTAs in Florida. Of these, 79.9% were male, 45.0% non-Hispanic Black, and 31.1% aged 25-34 years. The majority were men who have sex with men (MSM) (56.8%) and resided in an urban area (98.3%). The annual number of new diagnoses ranged from 2287 to 2351 during 2014–2018. The distribution of individual- and neighborhood-level characteristics were similar across 2014–2018, as shown in Table 1.

Overall, persons diagnosed with HIV during 2014–2018 were infected for a median duration of 83.0 (IQR: 42.0, 150.0) months prior to the reported date of initial diagnosis. The median time infected at HIV diagnosis during 2014 and 2018 was 89.0

(IQR: 44.0, 163.0) and 80.0 (IQR: 40.0, 146.5) months, respectively. The EAPC was -2.4% (95% CI: -8.8, 4.5), indicating that the median time from HIV infection to diagnosis was stable during 2014–2018 (Figure 1).

Longer median time from HIV infection to diagnosis was seen in older persons: 35-44 (92.0 months [IQR: 44.0, 178.0]); 45-54 (97.0 [42.0, 170.0]); and 55 years and older (98.0 [54.0, 152.0]), women (92.0 [43.0, 165.0]), and non-Hispanic Blacks (87.0 [44.0, 163.0]) compared with non-Hispanic Whites (81.0 [39.0, 146.0]). Median time from HIV infection to diagnosis was longer in individuals with infection attributed to male (105.0 [51.0, 188.5]) and female heterosexual contact (93.0 [43.0, 170.0]) compared with MSM (76.0 [40.0, 132.0]). Individuals residing in rural areas (97.0 [48.0, 175.0]) had a longer median time than urban areas (83.0 [42.0, 150.0]). In rural areas, there was an increase in the median time from 101.5 months in 2014 to 121.5 months in 2018 (EAPC: 8.3 [95% CI: 1.9, 15.0]). The longest median time from HIV infection to diagnosis was in neighborhoods with >10.4% of the population aged ≥ 16 who were unemployed (quartile 4) (83.0 [43.0, 154.0]), 14.6-20.7% of the population aged ≥ 25 with less than a 12^{th}-grade education (quartile 3) (87.0 [43.0, 156.0]), 33.1-45.5% households living in rented housing (quartile 2) (87.0 [43.0, 158.0]), and 10.7-14.3% of households with an annual income <$15,000 (quartile 2) (86.0 [43.0, 153.0]). Table 2 shows the median length of time from HIV infection to diagnosis, stratified by selected variables during 2014–2018.

Overall, 23.8% of PWH were diagnosed within 40 months of HIV infection (Table 3). Lower percentages of individuals aged 55+ years (17.0%), females (23.0%), non-Hispanic Blacks (22.2% vs. non-Hispanic Whites [26.2%]), and heterosexual males (19.1% vs. MSM [25.2%]) were diagnosed within 40 months. We observed minimal variability in the proportion of individuals diagnosed within 40 months for the neighborhood-level variables (22.2% to 25.9%).

In the multivariable analyses, individuals more likely to be diagnosed with HIV within 40 months were aged 13-19 (HR 1.65, 95% CI: 1.31, 2.06), 20-24 (1.53 [1.30, 1.79]), 25-34 (1.55 [1.35, 1.79[), 35-44 (1.36 [1.17, 1.58]) and 45-54 years (1.46 [1.25, 1.69]) compared with 55 years and older. Further, MSM/IDU (1.51 [1.20, 1.91]) compared with MSM and residing in an area where 9.7-14.5% of the residents had low education (quartile 2) (1.16, [1.05, 1.29]) compared with the 1st quartile were more likely to be diagnosed with HIV within 40 months. Compared with non-Hispanic Whites, non-Hispanic Blacks (HR 0.84, 95% CI 0.77, 0.93) and Others (HR 0.56, 95% CI 0.42, 0.75) were less likely to be diagnosed within 40 months as were heterosexual men relative to MSM (HR 0.75, 95% CI 0.67, 0.84). The variance of the frailty distribution was 0.002 ($p > 0.05$), suggesting a lack of variation in receiving a diagnosis within 40 months by census tract. We did not find any meaningful differences in the AHR and levels of statistical significance between the log-normal and the gamma frailty models (data not shown).

In post-hoc analyses, we fitted a parallel set of models by censoring individuals who did not receive an HIV diagnosis at a cut-off of 83 months, corresponding to the median time from HIV infection to diagnosis estimated for the study population. Although we observed changes in the magnitude of the AHRs in the multivariable analysis, we arrived at the same conclusion except for a few exceptions where there were meaningful differences: a different level of statistical significance was seen in HIV mode of transmission category (IDU [AHR 1.18, 95% CI 1.01, 1.38] vs. MSM), high rented housing: >58.2% (1.14 [1.03, 1.27] vs. 0-33.0%), and low education: 9.7-14.5% (1.07 [0.98,1.16] vs. 0-9.6%) (Supplemental Table 1).

Discussion

Our analysis of 5 years of population-based surveillance data using a CD4-depletion model provides additional insight into the epidemiologic profile of PWH in Florida. We estimated that one-half of individuals were infected with HIV for over 83 months before their diagnosis during 2014-2018. While the median time from HIV infection to diagnosis differed across subgroups, our analysis suggests no evidence of a decline over the 5-year study period. Being younger or middle-aged, MSM/Male IDU mode of transmission or residing in a census tract where 9.7-14.5% of residents had low education (quartile 2) was associated with diagnosis within 40 months after HIV infection. Non-Hispanic Blacks and heterosexual males were less likely to have HIV diagnosed closer to the time of infection.

Notably, the median time from HIV infection to diagnosis found in our study (83 months) was markedly longer than that reported in other studies (Crepaz et al., 2021; Hall et al., 2015; Peruski et al., 2021; Robertson et al., 2020). However, the stability in the time from infection to diagnosis over the study period observed was similar to other studies. For example, a recent U.S. national study of PWH residing in the 50 states and District of Columbia also reported that the median time from infection to diagnosis remained unchanged from 2014 to 2018 (Peruski et al., 2021). Similarly, in New York City, the median time from HIV diagnosis was stable from 2011 to 2015 (Robertson et al., 2020). In contrast, a study of 33 U.S. jurisdictions found, on average, a 1.5% decline in the median time to HIV diagnosis from 2014 to 2018 (Crepaz et al., 2021). Late detection of HIV infection may indicate lower testing rates in specific areas or groups, or barriers to care. The higher HIV burden and prevalence of social inequities impacting the HIV epidemic in Florida may explain the longer time from HIV infection to diagnosis compared to other populations (Jeffries & Henny, 2019). Additionally, the geographical

variation and the diverse demographic and sexual risk characteristics of the HIV population in Florida impose additional complexities to managing the epidemic (Florida Department of Health. Bureau of Communicable Diseases, 2022). Various federal-, state- and county-level comprehensive prevention strategies have been developed and implemented over the years to bring the epidemic under control in Florida (Centers for Disease Control and Prevention, 2019b; Miami-Dade HIV/AIDS Partnership, 2017). For example, in 2014, the Florida State Department of Health was one of the four health departments designated to receive funding from the CDC for three years in the Partnerships for Care project (Centers for Disease Control and Prevention, 2019b). One of the goals of this project was for CDC-funded state health departments and Health Resources and Services Administration-funded health centers to collaborate to improve the early detection of undiagnosed HIV infection. As another example, partnerships between the Florida Department of Health, county officials, and HIV prevention stakeholders in Miami-Dade County led to the development of specific goals and recommendations to improve and prioritize HIV testing and prevention strategies for the local community (Miami-Dade HIV/AIDS Partnership, 2017). Given all these efforts combined, it is likely that case finding yields of late-diagnosed PWH from efficient routine testing strategies may have reached a plateau in improving time to diagnosis. As such, the median time from HIV to diagnosis remained stable over the years in our study.

Individual-level characteristics linked with the length of time from HIV infection to diagnosis that we observed are mostly consistent with previous research. Similar to other studies (Crepaz et al., 2021; Dailey et al., 2017; Hall et al., 2015; Robertson et al., 2020), we found longer time from HIV infection to diagnosis in older adults than their younger counterparts. Moreover, studies have shown that late diagnosis measured as having AIDS within 3 months of HIV diagnosis is more prevalent among older adults

(Hall et al., 2016; Trepka et al., 2014). Given that older adults have lived longer, it is unlikely that younger persons, particularly those in the lowest age groups, would have been infected longer. In a separate analysis, we examined a crosstabulation between HIV transmission category and age group. While the majority of the younger age groups (13-19, 20-24, and 25 -34 years) were MSM (65.4% to 74.4%), in the 55+ age group, 22.7% and 30.0% were heterosexual males and MSM, respectively. Given that heterosexual males were more likely to have longer median time to diagnosis than MSM in our study, it is not surprising that we found longer time in older adults. Consistent with other studies in other U.S. jurisdictions (Crepaz et al., 2021; Peruski et al., 2021) and high-income countries (Kirby Institute, 2018; Nash et al., 2018; van Sighem et al., 2018), the majority of new HIV diagnoses in our study were in MSM. Several studies (Crepaz et al., 2021; Dailey et al., 2017; Hall et al., 2015; Peruski et al., 2021; Robertson et al., 2020) also report similar findings of longer median time to diagnosis among heterosexual males than MSM. Because the HIV epidemic disproportionately affects MSM (Centers for Disease Control and Prevention, 2021), HIV testing and prevention strategies have concentrated efforts on MSM (Centers for Disease Control and Prevention, 2011, 2013, 2019c; U.S. Department of Health and Human Services, 2014), potentially leaving heterosexuals behind. HIV testing in MSM has dramatically increased over time relative to other transmission risk groups (Dailey et al., 2017). According to a systematic review of outreach HIV testing in resource-rich countries, the most frequently tested group was MSM (Thornton et al., 2012). Another contributing factor could also be that health care providers perceive heterosexuals as low risk of HIV acquisition and therefore, offer this group fewer opportunities to get tested (Pringle et al., 2013).

It is worth noting that non-Hispanic Blacks are more likely to undergo HIV testing compared with Whites (Gaines et al., 2016; Lo et al., 2018). In an analysis of data from

the National Health Interview Survey, researchers reported higher adjusted odds of lifetime HIV testing among Blacks relative to Whites (Lo et al., 2018). Another study using the 2012 BRFSS survey data found that Blacks were more likely to have tested within the past 12 months when compared with other racial/ethnic groups (Gaines et al., 2016). Yet, we found longer median time to diagnosis for non-Hispanic Blacks than non-Hispanic Whites in our study, but not for Hispanics. It may be that Blacks are testing, but not regularly enough to capture HIV early. More minorities than Whites live in areas with high concentrations of low-income residents, a trend that is expected to exacerbate already existing racial health inequities (Gant et al., 2014; Vaughan et al., 2014). Previous research revealed relationships between neighborhood-level poverty and HIV outcomes (Cope et al., 2020; Joy et al., 2008; McDavid Harrison et al., 2008; Wiewel et al., 2017). Neighborhood-level poverty deprives people of critical resources such as education, economic opportunities, housing, and healthcare (Diez Roux, 2001), which may negatively impact their health-seeking behavior. Our findings suggest racial disparities in late HIV diagnosis and future areas for HIV preventive research, particularly among non-Hispanic Blacks.

Our study is not without limitations. First, our estimates were based on individuals who had at least one CD4 and viral load measurement. As a result, we excluded individuals with missing data and did not use imputation to address this issue. Multiple imputation is valid if its assumptions are valid. Given that we were unsure of the nature of the missingness of the data, we chose not to apply this approach. Therefore, our estimates of time from HIV to diagnosis may be overestimated or underestimated. Estimates of time from HIV to diagnosis may be underestimated or overestimated if the date of first HIV diagnosis is erroneous or inaccuracies in the CD4 counts reported. Second, the factors that contribute to early or delayed diagnosis are numerous. For

instance, having a mental illness or engaging in heavy drinking has been associated with more frequent HIV testing, both of which can lead to risky behavior linked to HIV exposure (Huang et al., 2008; Ostermann et al., 2007; Yehia et al., 2014). Psychosocial factors are not typically available in HIV surveillance data; therefore, we were unable to examine these factors as determinants of length of time from HIV infection to diagnosis. Third, when residential ZIP codes are used to define neighborhoods, geographical misrepresentation can occur, as individuals often interact outside the ZIP codes' geographic limits (Duncan et al., 2014).

Conclusion

Our study indicates that a substantial number of individuals lived with HIV for a long time before their diagnosis and the median time between infection and diagnosis did not decrease from 2014 to 2018. Novel strategies to increase access to HIV testing, including promoting screening in other alternative settings such as workplaces as well as ensuring HIV-self testing kits are readily available to the hard-to-reach population, may be beneficial. Further research to determine which approaches are most effective in increasing HIV testing access in diverse settings with varying local needs can help shape additional ways to close the gaps in early diagnosis of HIV.

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Table 1. Characteristics of persons aged ≥13 years diagnosed with HIV during 2014 – 2018, Florida

	Total N (%)	2014 n (%)	2015 n (%)	2016 n (%)	2017 n (%)	2018 n (%)
Total	11566	2333	2351	2287	2333	2252
Individual-level variables						
Age at diagnosis (years)						
13-19	420 (3.6)	71 (3.0)	93 (4.0)	83 (3.6)	92 (3.8)	81 (3.6)
20-24	1648 (14.3)	352 (15.1)	362 (15.4)	319 (14.0)	322 (13.4)	293 (13.0)
25-34	3593 (31.1)	694 (29.8)	681 (29.0)	711 (31.1)	746 (31.0)	761 (33.8)
35-44	2346 (20.3)	453 (19.4)	481 (20.5)	490 (21.4)	468 (20.0)	454 (20.2)
45-54	2148 (18.6)	493 (21.1)	448 (19.1)	403 (17.6)	413 (18.1)	391 (17.4)
55+	1401 (12.1)	270 (11.6)	286 (12.2)	281 (12.3)	292 (13.7)	272 (12.1)
Sex at birth						
Male	9122 (79.0)	1834 (76.6)	1854 (78.9)	1790 (78.3)	1854 (79.6)	1790 (79.5)
Female	2434 (21.1)	499 (21.4)	497 (21.1)	497 (21.7)	479 (20.4)	462 (20.5)
Race/ethnicity						
Non-Hispanic Black	5191 (45.0)	1087 (46.6)	1089 (46.3)	1050 (45.9)	1047 (44.9)	918 (40.8)
Hispanic	3430 (29.7)	630 (27.0)	678 (28.8)	684 (29.9)	693 (29.7)	745 (33.1)
Non-Hispanic White	2646 (22.9)	553 (23.7)	528 (22.5)	494 (21.6)	535 (22.9)	535 (23.8)
Other	289 (2.5)	63 (2.7)	56 (2.4)	59 (2.6)	58 (2.5)	53 (2.4)
HIV transmission category						
MSM	6558 (56.8)	1313 (56.3)	1358 (57.8)	1305 (57.1)	1337 (57.3)	1245 (55.3)
Male IDU	213 (1.8)	45 (1.9)	45 (1.9)	33 (1.4)	36 (1.5)	54 (2.4)
MSM + Male IDU	218 (1.9)	45 (1.9)	43 (1.8)	47 (2.1)	39 (1.7)	44 (2.0)

Heterosexual male	1772 (15.3)	376 (16.1)	351 (15.0)	347 (15.2)	340 (14.6)	358 (15.0)
Male - Other	532 (4.6)	102 (4.4)	82 (3.5)	87 (3.8)	157 (6.7)	104 (4.6)
Heterosexual female	2063 (17.9)	418 (17.9)	433 (18.4)	432 (18.9)	393 (16.9)	387 (17.2)
Female IDU	174 (1.5)	34 (1.5)	38 (1.6)	35 (1.5)	31 (1.3)	36 (1.6)
Female - Other	26 (0.2)	0	1 (0.0)	1 (0.0)	0	24 (1.1)
ZCTA-level variables						
RUCA classification						
Rural	200 (1.7)	42 (1.8)	39 (1.7)	38 (1.7)	33 (1.4)	48 (2.1)
Urban	11356 (98.3)	2291 (98.2)	2312 (98.3)	2249 (98.3)	2300 (98.6)	2204 (97.9)
[a]High unemployment						
Q1 (0 - 5.8)	2923 (25.3)	576 (24.7)	622 (26.5)	601 (26.3)	574 (24.6)	550 (24.4)
Q2 (5.9 - 7.8)	2962 (25.6)	582 (25.0)	561 (23.9)	597 (26.1)	619 (26.5)	603 (26.8)
Q3 (7.9 - 10.4)	2856 (24.7)	590 (25.3)	569 (24.2)	552 (24.1)	572 (24.5)	573 (25.4)
Q4 (>10.4)	2815 (24.4)	585 (25.1)	599 (25.5)	537 (23.5)	568 (24.4)	526 (23.4)
[b]Low education						
Q1 (0 - 9.6)	2940 (25.4)	589 (25.3)	601 (25.6)	582 (25.5)	610 (26.2)	558 (24.8)
Q2 (9.7 - 14.5)	2839 (24.6)	559 (24.0)	583 (24.8)	552 (24.1)	557 (23.9)	588 (26.1)
Q3 (14.6 - 20.7)	2945 (25.5)	624 (26.8)	559 (23.8)	582 (25.5)	597 (25.6)	583 (25.9)
Q4 (>20.7)	2832 (24.5)	561 (24.1)	608 (25.9)	571 (25.0)	569 (24.4)	523 (23.2)
[c]High rented housing						
Q1 (0 - 33.0)	2880 (24.9)	511 (21.9)	562 (23.9)	607 (26.5)	603 (25.9)	597 (26.5)
Q2 (33.1 - 45.5)	2970 (25.7)	650 (27.9)	587 (25.0)	569 (24.9)	580 (24.9)	584 (25.9)
Q3 (45.6 - 58.2)	2833 (24.5)	603 (25.9)	561 (23.9)	551 (24.1)	571 (24.5)	547 (24.3)
Q4 (>58.2)	2873 (24.9)	569 (24.4)	641 (27.3)	560 (24.5)	579 (24.8)	524 (23.3)

[d]Low household income						
Q1 (0 - 10.6)	2960 (25.6)	565 (24.2)	568 (24.2)	598 (26.2)	639 (27.4)	590 (26.2)
Q2 (10.7 - 14.3)	2820 (24.4)	566 (24.3)	570 (24.3)	580 (25.4)	567 (24.3)	537 (23.9)
Q3 (14.4 - 19.0)	2879 (24.9)	603 (25.9)	595 (25.3)	549 (24.0)	558 (23.9)	574 (25.5)
Q4 (>19.0)	2897 (25.1)	599 (25.7)	618 (26.3)	560 (24.5)	569 (24.4)	551 (24.5)

Abbreviations: MSM: men who have sex with men; IDU: injection drug use; RUCA: rural-urban commuting area; ZCTA: ZIP Code Tabulation Areas

[a]High unemployment is defined as the percent of the population aged ≥ 16 who were unemployed

[b]Low education is defined as the percent of the population aged ≥ 25 with less than a 12th-grade education

[c]High rented housing is defined as the percent of households living in rented housing

[d]Low household income is defined as the percent of households with an annual income <$15,000

Note: Q1 - Q4 represent 1st (lowest) to 4th (highest) quartiles. Percentages represent column percentages.

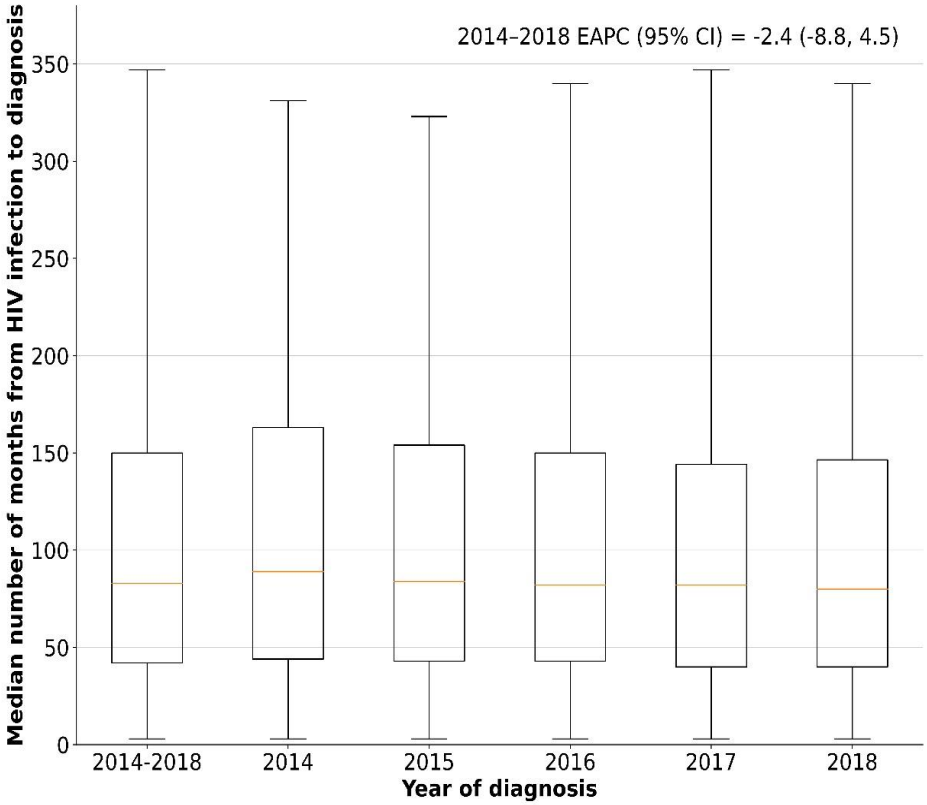

Fig 1. Median number of months infected at HIV diagnosis, 2014–2018, Florida. Box plot of 25th percentile, median, and 75th percentile, with whiskers.

*EAPC (Estimated annual percent change) indicates the per-year change from 2014-2018, on average, in the median time from HIV infection to diagnosis and its

Table 2. Estimated median number of months from HIV infection to diagnosis among persons aged ≥13 Years during 2014 – 2018, Florida

	Overall	2014	2015	2016	2017	2018	2014–2018 EAPC[a] (95% CI)
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	
Individual-level variables Age at diagnosis (years)							
13-19	67.5 (39.0, 102.0)	82.0 (41.0, 110.0)	77.0 (45.0, 106.0)	56.0 (38.0, 102.0)	64.5 (32.0, 101.0)	66.0 (38.0, 96.0)	-6.3 (-13.1, 1.0)
20-24	67.5 (40.0, 107.5)	73.0 (45.0, 120.0)	69.0 (38.0, 107.0)	65.0 (39.0, 109.0)	68.5 (38.0, 103.0)	63.0 (40.0, 95.0)	-3.1 (-10.1, 4.5)
25-34	76.0 (39.0, 145.0)	83.0 (37.0, 157.0)	73.0 (39.0, 153.0)	75.0 (42.0, 140.0)	76.5 (36.0, 138.0)	76.0 (41.0, 142.0)	-1.4 (-8.1, 5.9)
35-44	92.0 (44.0, 178.0)	102.0 (47.0, 195.0)	95.0 (44.0, 181.0)	96.0 (49.0, 179.0)	85.5 (46.0, 166.0)	83.5 (36.0, 172.0)	-4.9 (-10.9, 1.4)
45-54	97.0 (42.0, 170.0)	93.0 (40.0, 179.0)	105.5 (48.0, 170.5)	102.0 (41.0, 171.0)	92.0 (41.0, 160.0)	96.0 (41.0, 171.0)	-0.8 (-6.8, 5.7)
55+	98.0 (54.0, 152.0)	106.0 (67.0, 155.0)	99.5 (54.0, 152.0)	98.0 (51.0, 150.0)	95.0 (50.5, 154.5)	86.0 (44.0, 151.0)	-4.5 (-10.3, 1.7)
Sex at birth							
Male	82.0 (42.0, 147.0)	86.0 (44.0, 158.0)	82.0 (43.0, 150.0)	81.0 (42.0, 142.0)	80.0 (41.0, 143.0)	77.0 (40.0, 142.0)	-2.4 (-8.9, 4.5)
Female	92.0 (43.0, 165.0)	94.0 (43.0, 170.0)	92.0 (45.0, 167.0)	94.0 (49.0, 175.0)	85.0 (39.0, 155.0)	90.5 (41.0, 160.0)	-1.6 (-7.8, 5.0)
Race/ethnicity							
Non-Hispanic Black	87.0 (44.0, 163.0)	98.0 (47.0, 177.0)	87.0 (45.0, 169.0)	87.0 (45.0, 164.0)	84.0 (42.0, 149.0)	83.5 (42.0, 154.0)	-3.7 (-9.9, 2.9)
Hispanic	78.0 (40.0, 138.0)	74.0 (39.0, 132.0)	79.0 (41.0, 143.0)	80.0 (43.0, 140.0)	80.0 (40.0, 142.0)	74.0 (40.0, 134.0)	0.1 (-6.7, 7.4)
Non-Hispanic White	81.0 (39.0, 146.0)	85.0 (42.0, 150.0)	82.5 (42.0, 145.0)	82.0 (39.0, 149.0)	71.0 (36.0, 139.0)	79.0 (36.0, 147.5)	-2.8 (-9.4, 4.1)
Other	97.0 (57.0, 165.0)	126.0 (76.0, 182.0)	96.5 (63.5, 151.5)	97.0 (49.0, 166.0)	91.0 (52.0, 171.0)	94.0 (60.0, 152.0)	**-6.6 (-12.2, -0.7)**
HIV transmission category							
MSM	76.0 (40.0, 132.0)	80.0 (42.0, 143.0)	76.0 (41.0, 136.0)	75.0 (40.0, 133.0)	75.0 (38.0, 129.0)	72.0 (40.0, 126.0)	-2.2 (-9.0, 5.0)
Male IDU	82.0 (37.0, 141.0)	92.0 (51.0, 144.0)	88.0 (34.0, 130.0)	62.0 (36.0, 125.0)	88.5 (49.0, 143.5)	68.0 (32.0, 155.0)	-5.8 (-12.1, 1.0)
MSM + Male IDU	63.5 (29.0, 120.0)	66.0 (38.0, 127.0)	65.0 (32.0, 115.0)	65.0 (30.0, 120.0)	69.0 (26.0, 136.0)	41.5 (24.0, 107.5)	-7.3 (-14.3, 0.4)

Heterosexual male	105.0 (51.0, 188.5)	108.5 (56.0, 201.0)	112.0 (55.0, 183.0)	108.0 (52.0, 193.0)	94.0 (46.5, 183.5)	104.0 (44.0, 181.0)	-2.5 (-8.2, 3.5)
Male - Other	128.0 (59.0, 205.0)	143.0 (83.0, 218.0)	125.5 (69.0, 205.0)	155.0 (85.0, 231.0)	122.0 (58.0, 183.0)	97.0 (34.0, 200.5)	**-7.1 (-12.1, -1.9)**
Heterosexual female	93.0 (43.0, 170.0)	94.0 (43.0, 173.0)	95.0 (44.0, 172.0)	97.0 (45.0, 176.5)	87.0 (40.0, 161.0)	91.0 (41.0, 162.0)	-1.5 (-7.6, 5.0)
Female IDU	63.0 (38.0, 94.0)	49.0 (35.0, 100.0)	62.5 (43.0, 95.0)	65.0 (50.0, 80.0)	51.0 (31.0, 77.0)	72.5 (36.5, 117.0)	6.1 (-2.1, 15.0)
Female - Other	123.5 (47.0, 229.0)	0	129.0 (129.0, 129.0)	60.0 (60.0, 60.0)	0	127.0 (44.0, 236.5)	**22.3 (12.9, 32.5)**
ZCTA-level variables							
RUCA classification							
Rural	97.0 (48.0, 175.0)	101.5 (38.0, 177.0)	73.0 (38.0, 117.0)	117.5 (54.0, 192.0)	117.0 (54.0, 174.0)	121.5 (59.5, 175.0)	**8.3 (1.9, 15.0)**
Urban	83.0 (42.0, 150.0)	89.0 (44.0, 162.0)	85.0 (43.0, 154.0)	82.0 (43.0, 149.0)	81.0 (40.0, 144.0)	79.0 (40.0, 145.5)	-2.8 (-9.2, 4.0)
[b]High unemployment							
Q1 (0 - 5.8)	81.0 (40.0, 141.0)	82.0 (38.0, 144.0)	82.0 (42.0, 139.0)	79.0 (39.0, 138.0)	81.0 (40.0, 142.0)	82.5 (42.0, 138.0)	0 (-6.6, 7.1)
Q2 (5.9 - 7.8)	84.0 (43.0, 152.0)	92.0 (46.0, 164.0)	81.0 (42.0, 148.0)	84.0 (44.0, 162.0)	83.0 (44.0, 145.0)	78.0 (38.0, 147.0)	-3.1 (-9.4, 3.7)
Q3 (7.9 - 10.4)	86.0 (42.0, 157.0)	94.0 (45.0, 179.0)	85.0 (41.0, 163.0)	92.5 (50.0, 160.0)	85.0 (42.0, 147.0)	79.0 (37.0, 143.0)	-3.4 (-9.6, 3.3)
Q4 (>10.4)	83.0 (43.0, 154.0)	85.0 (45.0, 158.0)	92.0 (47.0, 167.0)	79.0 (41.0, 139.0)	76.0 (36.0, 144.5)	78.0 (43.0, 151.0)	-3.6 (-10.0, 3.2)
[c]Low education							
Q1 (0 -9.6)	83.0 (43.0, 149.0)	91.0 (44.0, 156.0)	81.0 (42.0, 139.0)	83.0 (43.0, 152.0)	80.0 (44.0, 143.0)	84.0 (43.0, 150.0)	-1.8 (-8.2, 5.1)
Q2 (9.7 - 14.5)	81.0 (39.0, 150.0)	84.0 (36.0, 160.0)	84.0 (42.0, 159.0)	81.5 (45.5, 146.0)	76.0 (35.0, 144.0)	78.5 (38.0, 146.0)	-2.3 (-8.8, 4.7)
Q3 (14.6 - 20.7)	87.0 (43.0, 156.0)	100.0 (49.0, 173.5)	88.0 (46.0, 156.0)	80.5 (44.0, 154.0)	86.0 (42.0, 148.0)	80.0 (37.0, 146.0)	-4.7 (-10.9, 1.8)
Q4 (>20.7)	82.5 (43.0, 146.5)	82.0 (44.0, 150.0)	85.0 (44.0, 156.0)	86.0 (41.0, 144.0)	82.0 (42.0, 143.0)	75.0 (42.0, 138.0)	-2.1 (-8.5, 4.9)
[d]High rented housing							
Q1 (0 - 33.0)	86.0 (44.0, 155.0)	95.0 (46.0, 163.0)	84.5 (45.0, 163.0)	87.0 (46.0, 157.0)	80.0 (40.0, 143.0)	85.0 (42.0, 157.0)	-2.8 (-9.1, 3.9)
Q2 (33.1 - 45.5)	87.0 (43.0, 158.0)	92.0 (44.0, 176.0)	89.0 (45.0, 152.0)	91.0 (45.0, 160.0)	81.5 (39.0, 152.0)	81.0 (39.5, 149.0)	-3.3 (-9.6, 3.3)

Q3 (45.6 - 58.2)	83.0 (42.0, 152.0)	83.0 (43.0, 160.0)	81.0 (41.0, 152.0)	86.0 (43.0, 146.0)	92.0 (46.0, 162.0)	74.0 (38.0, 138.0)	-0.8 (-7.4, 6.1)
Q4 (>58.2)	79.0 (40.0, 138.0)	85.0 (41.0, 152.0)	82.0 (42.0, 151.0)	71.0 (38.0, 133.0)	71.0 (36.0, 129.0)	79.0 (41.0, 133.0)	-2.9 (-9.5, 4.2)
[e]Low household income							
Q1 (0 - 10.6)	86.0 (44.0, 153.0)	98.0 (45.0, 164.0)	81.5 (43.0, 152.0)	85.0 (45.0, 154.0)	82.0 (44.0, 147.0)	84.0 (41.0, 147.0)	-3.1 (-9.4, 3.6)
Q2 (10.7 - 14.3)	84.0 (43.0, 153.0)	84.0 (41.0, 163.0)	89.0 (46.0, 154.0)	81.5 (44.5, 155.5)	81.0 (41.0, 145.0)	80.0 (41.0, 152.0)	-1.9 (-8.4, 5.0)
Q3 (14.4 - 19.0)	83.0 (40.0, 150.0)	85.0 (41.0, 163.0)	82.0 (41.0, 153.0)	82.0 (42.0, 145.0)	87.0 (39.0, 155.0)	80.0 (36.0, 137.0)	-0.6 (-7.1, 6.4)
Q4 (>19.0)	82.0 (42.0, 145.0)	89.0 (46.0, 155.0)	83.0 (42.0, 154.0)	81.5 (40.0, 146.5)	75.0 (37.0, 132.0)	75.0 (42.0, 140.0)	-4.4 (-10.8, 2.5)

Abbreviations: CI: confidence interval; EAPC: estimated annual percent change; IDU: injection drug use; IQR: interquartile range; MSM: men who have sex with men; RUCA: rural-urban commuting area

Note: Bolded values indicate statistical significance ($p<0.05$). Q1 - Q4 represent 1st to 4th quartiles.

[a]EAPC indicates the per-year change from 2014-2018, on average, in the median time from HIV infection to diagnosis

[b]High unemployment is defined as the percent of the population aged ≥ 16 who were unemployed

[c]Low education is defined as the percent of the population aged ≥ 25 with less than a 12th-grade education

[d]High rented housing is defined as the percent of households living in rented housing

[e]Low household income is defined as the percent of households with an annual income <$15,000

Table 3. Crude and adjusted hazard ratios and 95% confidence intervals for receiving a diagnosis within 40 months after HIV infection among persons aged ≥13 years during 2014 – 2018, Florida

Variables	Diagnosed within 40 months after infection		
	n (%)	*Model 1 HR (95% CI)	¶Model 2 AHR (95% CI)
[a]Total number of events (%)		2751 (23.8)	
Individual-level variables			
Age at diagnosis (years)			
13-19	113 (26.9)	**1.68 (1.35, 2.09)**	**1.65 (1.31, 2.06)**
20-24	424 (25.7)	**1.58 (1.36, 1.85)**	**1.53 (1.30, 1.79)**
25-34	936 (26.1)	**1.64 (1.43, 1.89)**	**1.55 (1.35, 1.79)**
35-44	523 (22.3)	**1.41 (1.22, 1.64)**	**1.36 (1.17, 1.58)**
45-54	517 (24.1)	**1.51 (1.30, 1.75)**	**1.46 (1.25, 1.69)**
55+	238 (17.0)	ref	ref
Sex at birth			
Female	560 (23.0)	0.98 (0.89, 1.07)	0.92 (0.72, 1.18)
Male	2191 (24.0)	ref	ref
Race/ethnicity			
Hispanic	862 (25.1)	0.96 (0.86, 1.05)	0.91 (0.82, 1.01)
Non-Hispanic Black	1152 (22.2)	**0.84 (0.77, 0.93)**	**0.83 (0.75, 0.92)**
Non-Hispanic White	692 (26.2)	ref	ref
Other	45 (15.6)	**0.56 (0.42, 0.75)**	**0.55 (0.41, 0.74)**
[b]HIV transmission category			
Heterosexual female	482 (23.4)	0.95 (0.86, 1.05)	1.15 (0.88, 1.50)
Heterosexual male	338 (19.1)	**0.75 (0.67, 0.84)**	**0.84 (0.74, 0.95)**
IDU	103 (26.6)	1.07 (0.87, 1.30)	1.16 (0.92, 1.46)
MSM	1653 (25.2)	ref	ref
MSM + Male IDU	76 (34.9)	**1.51 (1.20, 1.89)**	**1.51 (1.20, 1.91)**
Other	99 (17.7)	**0.68 (0.59, 0.79)**	**0.79 (0.67, 0.93)**
ZCTA- level variables			
RUCA classification			
Rural	43 (21.5)	0.96 (0.72, 1.28)	0.97 (0.72, 1.30)
Urban	2708 (23.9)	ref	ref
[c]High unemployment			
Q1 (0 - 5.8)	731 (25.0)	ref	ref
Q2 (5.9 - 7.8)	693 (23.4)	0.92 (0.83, 1.02)	0.93 (0.83, 1.04)

Q3 (7.9 - 10.4)	673 (23.6)	0.93 (0.84, 1.03)	0.92 (0.81, 1.05)
Q4 (>10.4)	654 (23.2)	0.93 (0.84, 1.04)	0.91 (0.78, 1.05)
[d]Low education			
Q1 (0 -9.6)	673 (22.9)	ref	ref
Q2 (9.7 - 14.5)	735 (25.9)	**1.16 (1.05, 1.29)**	**1.15 (1.02, 1.29)**
Q3 (14.6 - 20.7)	686 (23.3)	1.03 (0.93, 1.14)	1.03 (0.90, 1.18)
Q4 (>20.7)	657 (23.2)	1.06 (0.96, 1.18)	1.04 (0.89, 1.22)
[e]High rented housing			
Q1 (0 - 33.0)	638 (22.2)	ref	ref
Q2 (33.1 - 45.5)	704 (23.7)	1.08 (0.97, 1.20)	1.08 (0.96, 1.22)
Q3 (45.6 - 58.2)	673 (23.8)	1.08 (0.97, 1.20)	1.08 (0.95, 1.22)
Q4 (>58.2)	736 (25.6)	**1.20 (1.08, 1.33)**	1.14 (0.99, 1.32)
[f]Low household income			
Q1 (0 - 10.6)	662 (22.4)	ref	ref
Q2 (10.7 - 14.3)	657 (23.3)	1.05 (0.94, 1.17)	1.03 (0.91, 1.17)
Q3 (14.4 - 19.0)	736 (25.6)	**1.16 (1.05, 1.29)**	1.10 (0.95, 1.26)
Q4 (>19.0)	696 (24.0)	1.11 (1.00, 1.24)	1.12 (0.94, 1.35)
[g]Variance			0.01393

Abbreviations: AHR: adjusted hazard ratio; CI: confidence interval; HR: crude hazard ratio; IDU: injection drug use; IQR: interquartile range; MSM: men who have sex with men; RUCA: rural-urban commuting area; ZCTA: ZIP Code Tabulation Areas

Note: Bolded values indicate statistical significance ($p<0.05$). Q1 - Q4 represent 1st to 4th quartiles. -- indicates variables that were dropped during the stepwise selection procedure

[a]Individuals were right-censored depending on whether they exceeded the threshold set for the time from HIV infection to diagnosis (i.e., 40 months)

[b]HIV transmission category was recoded into 6 levels. IDU included both men (n=213) and women (n=174) and Other included both men (n=532) and women (n=26)

[c]High unemployment is defined as the percent of the population aged ≥ 16 who were unemployed

[d]Low education is defined as the percent of the population aged ≥ 25 with less than a 12th-grade education

[e]High rented housing is defined as the percent of households living in rented housing

[f]Low household income is defined as the percent of households with an annual income <$15,000

[g]Variance estimate of the random effects

*Model 1 - Univariable Cox proportional hazard model

¶Model 2 - Multivariable Cox proportional hazard model including individual- and neighborhood-level variables and a random component (frailty term) using a log-normal distribution

Supplemental Table 1. Crude and adjusted hazard ratios and 95% confidence intervals for likelihood of diagnosis after HIV infection among persons aged ≥13 Years during 2014 – 2018, Florida

Variables	Diagnosed within 83 months after infection		
	n (%)	*Model 1 HR (95% CI)	¶Model 2 AHR (95% CI)
[b]Total number of events (%)		5779 (50.0)	
Individual-level variables			
Age at diagnosis (years)			
13-19	254 (60.5)	**1.74 (1.50, 2.01)**	**1.61 (1.39, 1.87)**
20-24	1023 (62.1)	**1.79 (1.62, 1.98)**	**1.64 (1.48, 1.82)**
25-34	1905 (53.0)	**1.50 (1.37, 1.64)**	**1.36 (1.24, 1.49)**
35-44	1074 (45.8)	**1.22 (1.11, 1.35)**	**1.16 (1.05, 1.28)**
45-54	952 (44.3)	**1.19 (1.08, 1.32)**	**1.13 (1.02, 1.25)**
55+	571 (40.8)	ref	ref
Sex at birth			
Female	1120 (46.0)	**0.89 (0.83, 0.94)**	1.08 (0.91, 1.29)
Male	4659 (51.1)	ref	ref
Race/ethnicity			
Hispanic	1818 (53.0)	1.03 (0.96, 1.11)	0.98 (0.91, 1.05)
Non-Hispanic Black	2480 (47.8)	**0.90 (0.84, 0.96)**	**0.89 (0.83, 0.96)**
Non-Hispanic White	1363 (51.5)	ref	ref
Other	118 (40.8)	**0.68 (0.56, 0.82)**	**0.66 (0.55, 0.80)**
[b]HIV transmission category			
Heterosexual female	938 (45.5)	**0.81 (0.75, 0.87)**	0.83 (0.69, 1.01)
Heterosexual male	717 (40.5)	**0.68 (0.63, 0.74)**	**0.77 (0.71, 0.84)**
IDU	227 (58.7)	1.11 (0.97, 1.27)	**1.18 (1.01, 1.38)**
MSM	3577 (54.5)	ref	ref
MSM + Male IDU	131 (60.1)	**1.24 (1.04, 1.48)**	**1.32 (1.10, 1.57)**
Other	189 (33.9)	**0.54 (0.49, 0.60)**	**0.61 (0.54, 0.69)**
ZCTA- level variables			
RUCA classification			
Rural	91 (45.5)	0.90 (0.74, 1.10)	0.92 (0.75, 1.14)
Urban	5688 (50.1)	ref	ref
[c]High unemployment			
Q1 (0 - 5.8)	1505 (51.5)	ref	ref
Q2 (5.9 - 7.8)	1470 (49.6)	0.94 (0.87, 1.01)	0.95 (0.88, 1.03)

Q3 (7.9 - 10.4)	1387 (48.6)	**0.92 (0.86, 0.99)**	0.97 (0.88, 1.06)
Q4 (>10.4)	1417 (50.3)	0.97 (0.90, 1.04)	0.98 (0.88, 1.09)
[d]Low education			
Q1 (0 - 9.6)	1471 (50.0)	ref	ref
Q2 (9.7 - 14.5)	1463 (51.5)	1.07 (1.00, 1.15)	1.07 (0.98, 1.16)
Q3 (14.6 - 20.7)	1415 (48.1)	0.97 (0.90, 1.04)	1.00 (0.91, 1.10)
Q4 (>20.7)	1430 (50.5)	1.05 (0.98, 1.13)	1.07 (0.95, 1.19)
[e]High rented housing			
Q1 (0 - 33.0)	1400 (48.6)	ref	ref
Q2 (33.1 - 45.5)	1438 (48.42)	1.01 (0.94, 1.09)	1.03 (0.95, 1.12)
Q3 (45.6 - 58.2)	1423 (50.2)	1.06 (0.99, 1.14)	1.09 (1.00, 1.20)
Q4 (>58.2)	1518 (52.8)	**1.16 (1.08, 1.25)**	**1.14 (1.03, 1.27)**
[g]Low household income			
Q1 (0 - 10.6)	1454 (49.1)	ref	ref
Q2 (10.7 - 14.3)	1403 (49.8)	1.03 (0.95, 1.10)	1.01 (0.93, 1.11)
Q3 (14.4 - 19.0)	1449 (50.3)	1.04 (0.97, 1.12)	0.97 (0.88, 1.07)
Q4 (>19.0)	1473 (50.9)	1.08 (1.00, 1.15)	0.98 (0.86, 1.12)
[f]Variance			0.01253

Abbreviations: AHR: adjusted hazard ratio; CI: confidence interval; HR: crude hazard ratio; IDU: injection drug use; IQR: interquartile range; MSM: men who have sex with men; RUCA: rural-urban commuting area; ZCTA: ZIP Code Tabulation Areas

Note: Bolded values indicate statistical significance ($p<0.05$). Q1 - Q4 represent 1st to 4th quartiles. -- indicates variables that were dropped during the stepwise selection procedure

[a]Individuals were right-censored depending on whether they exceeded the threshold set for the time from HIV infection to diagnosis (i.e., 40 months)

[b]HIV transmission category was recoded into 6 levels. IDU included both men (n=213) and women (n=174) and Other included both men (n=532) and women (n=26)

[c]High unemployment is defined as the percent of the population aged ≥ 16 who were unemployed

[d]Low education is defined as the percent of the population aged ≥ 25 with less than a 12th-grade education

[e]High rented housing is defined as the percent of households living in rented housing

[f]Low household income is defined as the percent of households with an annual income <$15,000

[g]Variance estimate of the random effects

*Model 1 - Univariable Cox proportional hazard model

¶Model 2 - Multivariable Cox proportional hazard model including individual- and neighborhood-level variables and a random component (frailty term) using a log-normal distribution

MANUSCRIPT 2

A Comparative Analysis of Different HIV Viral Load Suppression Definitions among Clients Receiving Care in the Miami-Dade Ryan White HIV/AIDS Program

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Abstract

Differing definitions of viral load (VL) suppression have distinct clinical, epidemiologic, and programmatic implications. The study objective was to examine variations in viral suppression definitions and agreement between each definition among clients in the Miami-Dade County Ryan White Program (RWP). Data from clients enrolled in the RWP during 2017 were examined to calculate the proportion of virally suppressed clients using three definitions: recent viral suppression, defined as having a suppressed VL (<200 copies/mL) in the last test in 2017; maintained viral suppression, having a suppressed VL for both the first and last VL tests in 2017; and sustained viral suppression, having all VL measurements in 2017 showing suppression. Relative differences and 95% confidence intervals (CI) and Gwet's agreement coefficients (AC1) across all three definitions were computed. Recent viral suppression measures were higher than maintained and sustained viral suppression measures, by 7.0% and 10.1%, respectively. Significant relative differences in definitions by race/ethnicity, age, sex, household income, CD4 counts, and the number of VL tests performed were observed. Overall, non-Hispanic Blacks (0.88 [0.74-1.00]) and Haitians (0.87 [0.72-1.00]) had lower AC1 scores than Hispanics (0.94 [0.87-1.00]) and non-Hispanic Whites/Others (0.93 [0.82-1.00]) across all three definitions. Findings highlight variability in the estimates of viral suppression definitions, particularly across demographic, socioeconomic, and clinical status in the RWP. While recent viral suppression provides a point estimator for client outcomes while in care, it may be beneficial for care planning and evaluation of

ART effectiveness to report contextual VL data using maintained or sustained viral suppression as well.

Introduction

Plasma viral load (VL) is an essential biomarker in quantifying the viral burden among people with HIV (PWH) in clinical care, HIV programs, and research (Cohen et al., 2011; Mugavero et al., 2011; Quinn et al., 2000). Monitoring VL has demonstrated clinical value in determining treatment efficacy and the prognosis of PWH receiving care (Marschner et al., 1998; Murray et al., 1999). Patients with suppressed VL have decreased risk of morbidity and mortality (May et al., 2014) and HIV transmission potential (Crepaz et al., 2018, 2020). In national HIV programs (Health Resources and Services Administration, n.d.), the population-level assessment of viral suppression serves as a key indicator for evaluating quality performance measures that align with the National HIV/AIDS strategy goal (U.S. Department of Health and Human Services, 2021).

Although VL measures are typically obtained serially in practice, health care providers, researchers, and program implementers commonly use noncumulative values in analyses. For instance, the Ryan White HIV/AIDS Program (RWP) funding recipients utilize a single quantitative assessment to define viral suppression as having “less than 200 copies per mL at last HIV viral load test during the measurement year” when monitoring program clients’ outcomes (Department of Health and Human Services, 2019). While this single-value definition has been integral to client care (Marschner et al., 1998; Murray et al., 1999), its utility in capturing a client’s viral load dynamics over time is unknown. Some authors have argued that cumulative VL measures such as sustained viral suppression (Crepaz et al., 2018; Marks et al., 2016; Sheehan et al., 2020) may be more informative given fluctuations in VL that occur over time. Some

authors have used a matched-pairs method to determine patterns of changes in viral suppression status (Crepaz et al., 2017; Marks et al., 2016). In this approach, PWH who had both their first and last VL tests less than 200 copies per mL in a given year were classified as virally suppressed (Crepaz et al., 2017; Marks et al., 2016) without taking into account other VL tests performed that year.

Alternative definitions of viral suppression present distinct clinical, epidemiologic, and programmatic implications. Despite being classified as virally suppressed in a given year with a single-value definition, PWH may transmit HIV at other times of the year if their suppression status changes due to poor treatment adherence or changes in antiretroviral therapy (ART) medications (Skarbinski et al., 2015). Moreover, even some PWH successfully treated with highly active antiretroviral therapy experience intermittent viral blips (Percus et al., 2009) or long-term virological failure (Hull et al., 2009). Yet, few studies have assessed the comparability between definitions and their relevance in describing clients' viral burden.

We examined data of clients enrolled in the Miami-Dade County RWP Part A/Minority AIDS Initiative during calendar year 2017. The RWP is the payer of last resort that serves over 50% of all PWH in the United States with comprehensive HIV treatment, care, and support services (Centers for Disease Control and Prevention, 2020). Clients are eligible for services in the RWP if they are uninsured, underinsured, and below 400% of the current Federal Poverty Level (FPL). In 2017, the Miami–Fort Lauderdale–West Palm Beach Metropolitan Statistical Area of residence ranked first in the United States in the number of HIV and AIDS cases diagnosed among major metropolitan areas (Centers for Disease Control and Prevention, 2019a). An estimated 28,345 persons were living with HIV in Miami-Dade County by the end of 2018 at that time (Florida Department of Health, n.d.); the RWP provided services to 9,883 of these persons, over 35% of this

population (HIV/AIDS Partnership, 2019). We sought to: (1) examine how different definitions of viral suppression characterize PWH in the RWP, (2) quantify the degree of agreement between viral suppression definitions, and (3) identify demographic, behavioral, and clinical factors associated with each viral suppression definition among clients in the program. Our study aimed to understand how cumulative VL measures may improve the utility of viral suppression estimates to inform future policy.

Methods

Study Population and Design

We analyzed demographic, behavioral and laboratory data from clients (18 years or older) enrolled in the Miami-Dade County RWP. To be included in the analytic cohort, a client must be receiving medical case management services in the RWP, defined as having received at least one medical case management encounter before and during 2017. In addition, clients must have received at least one comprehensive health assessment in 2016 or 2017 to be included in analyses. Those who died within 2017, did not have an assessment available, were incarcerated, moved out of the county, or deemed financially ineligible, or had their files closed before the end of 2017 were excluded.

Viral Suppression Definitions

Clients with a VL test of <200 copies/mL were classified as suppressed, consistent with the national HIV program's threshold (Department of Health and Human Services, 2019). Three definitions of viral suppression were examined**.** *Recent viral suppression* was defined as having a suppressed VL in the last VL measurement in 2017 (Department of Health and Human Services, 2019). *Maintained viral suppression* was defined as evidence of suppressed VL in both the first and last VL tests in 2017 (Crepaz et al., 2017). For clients who had only one VL test in 2017 or more than one

test, but the test(s) were less than 90 days from the last VL test, we used the last VL in 2016 to define maintained viral suppression. Clients with one of the two VL tests not suppressed were defined as not maintained (Crepaz et al., 2017). *Sustained viral suppression* was defined as evidence of suppressed VL on all viral load tests in 2017 (Crepaz et al., 2018). For clients with only one VL test in 2017, or those with more than one test that were less than 90 days apart, and for whom the 2017 tests showed viral suppression, we looked at the last VL test in 2016 to define sustained viral suppression (Crepaz et al., 2018). If a client had any test in 2017 (or 2016 in cases when a 2016 measurement was needed) that was not suppressed, they were considered not to have achieved sustained viral suppression in 2017. Clients without a VL test in 2017 or those with only one suppressed VL test in 2017 and no VL test in 2016 were not included in analyses.

Demographic, Behavioral, and Clinical Variables

Race/ethnicity was grouped as Hispanic (at 54%, the largest ethnic group in care in the RWP in 2017), non-Hispanic Black, Hispanic, Haitian, and non-Hispanic White/Other (at 7.7%, the smallest ethnic group in care). “Other” accounted for 0.4% of the clients in care, and included Asians, Native American/Alaskan Natives, and Native Hawaiian/Pacific Islanders. Other variables included age, born in the United States, preferred language, household income level (percent of FPL), enrollment in the Affordable Care Act (ACA), earliest CD4 count in 2017, AIDS diagnosis (consistent with the CDC definition (Centers for Disease Control and Prevention, 2019b)) in 2017 (diagnosed prior to or anytime during 2017), and the number of VL results in 2017. Initial mode of HIV acquisition was a self-reported account of how an individual contracted HIV.

Data Analyses

All statistical analyses were performed using SAS/STATv14.2 (SAS Institute Inc, 2016). First, we examined the overall distributions of recent, maintained, and sustained viral suppression and conducted descriptive analyses of clients' characteristics by each viral suppression definition. We estimated the relative percent differences in proportions – a difference between pairs of viral suppression definitions divided by the value of the reference (for example, [(maintained – recent) / recent] x 100) along with its corresponding 95% confidence intervals (CI), overall and by client characteristics.

Second, we estimated simple percent agreement and the corresponding 95% CI. Simple percent agreement was defined as the percentage concordance in classifying clients as suppressed and not suppressed (for example, [(suppressed on both definitions + not suppressed on both definitions)/total sample]x100). Next, we used the MAGREE macro to estimate Gwet's first-order agreement coefficient (AC1) score (Gwet, 2014) to assess the degree of agreement among the three and between pairs of viral suppression definitions. Gwet's AC1, a chance-corrected index, has recently gained popularity in HIV (Font et al., 2020) and sexual health research (Sani et al., 2016; Ssewanyana et al., 2018) as it adjusts for a limitation of the less stable Kappa statistic coined the *Kappa paradox phenomenon* (Feinstein & Cicchetti, 1990; Gwet, 2014). The phenomenon states that in a situation with high likelihood of chance agreement among raters, high relative observed agreement produces low Kappa; whereas imbalanced marginal distributions yield greater Kappa (Cicchetti & Feinstein, 1990; Feinstein & Cicchetti, 1990). The strength of agreement was categorized according to Landis and Koch's (Landis & Koch, 1977) agreement classification as follows: < 0.2 = poor; 0.21–0.4 = fair; 0.41–0.6 = moderate; 0.61–0.8 = substantial; and 0.81–1.0 = almost perfect. In subgroup analyses, we explored these statistics by stratifying across racial/ethnic categories.

Third, we estimated positive predictive values (PPV) and negative predictive values (NPV) and corresponding 95% CI. When estimating PPVs/NPVs, we consecutively set each definition as the “reference standard” and compared it against the others (diagnostic tests) to better understand the interrelations between the definitions. Accordingly, we defined PPV as the proportion of clients classified as suppressed with respect to the reference standard, given the presence of suppression in the diagnostic test. Likewise, NPV was defined as the proportion of clients classified as not suppressed in the absence of suppression in the diagnostic test with respect to the reference standard.

Finally, we fitted a separate multiple logistic regression model to examine factors associated with each outcome definition. For the race/ethnicity variable, we decided *a priori* to employ the 'comparisons to the best group rate' (Talih & Huang, 2016) method to determine the reference group. Given that studies show that non-Hispanic Whites typically have the most favorable rates for viral suppression among all racial/ethnic groups, we selected non-Hispanic Whites/Other as our referent group. We checked for multicollinearity by successively examining correlations between each independent variable against the other. When we encountered collinearity between two variables ($r > 0.5$), we ran a univariable analysis for each variable with recent viral suppression as the outcome. We then selected the variable with the larger crude odds ratio for inclusion in the final models. For example, we found that being born in the United States and preferred language were highly correlated ($r=0.9$) and retained only the former for inclusion in the models. Using a forward stepwise procedure for each measure of viral suppression, we added potential explanatory variables sequentially if the 0.30 significance level for entry into the model was met and tested for statistical significance after each iteration. Variables with p-values not exceeding 0.35 were retained in the

models (Mickey & Greenland, 1989). We computed adjusted odds ratios (AOR) and stopped when the AOR was either reduced no further by adding additional variables to the model or did not meet the 0.35 significance level. We then used the z statistic to test whether there was a statistically significant difference in the log odds estimates of the factors for maintained and sustained viral suppression relative to recent viral suppression. This study was approved by the Florida International University Institutional Review Board.

Results

Study Population Characteristics

A total of 6,939 clients received medical case management in the Miami-Dade County RWP in 2017. Of these, 436 (6.3%) were removed from analyses because they had no VL tests in 2017 or only one VL test in 2017, and no VL test in 2016. The remaining analytic sample contained 6,503 clients with two or more VL tests, including the last VL in 2016 for 46 clients who had only one VL in 2017 or multiple VLs measured less than three months apart in that year. Of the 6,503 clients, 76.8% were male, 58.1% Hispanic, 24.3% non-Hispanic Black, 10.9% Haitian, and 6.6% non-Hispanic White/Other; 42.6% were 50 years or older, and the main risk factors for initial HIV acquisition were male-to-male sexual contact in 51.7% and heterosexual contact in 44.5%.

Viral Suppression Prevalence and Relative Differences between Definitions

Overall, 89.8% of clients were virally suppressed at their most recent VL test, 83.5% had maintained viral suppression, and 80.7% achieved sustained viral suppression in 2017 as shown in Table1. Comparing the proportions of recent and maintained viral suppression, we observed a relative difference of -7.0%. Similarly, we observed a relative reduction of 10.1% in the proportion for recent compared with

sustained viral suppression and 3.4% for maintained compared with sustained viral suppression.

Simple Percent Agreement

The simple percent agreement estimated according to the three definitions and each pairwise comparison stratified by racial/ethnic categories are depicted in Figure 1. For all three definitions, the overall simple percent agreement was 90.9%; among the racial/ethnic categories, it ranged from 87.2% in Haitians to 92.6% in Hispanics. Pairwise analyses showed the lowest levels of simple percent agreements of 87.2% to 92.6% between recent and sustained viral suppression definitions for the total sample and across the racial/ethnic categories. For the comparison between maintained and sustained viral suppression definitions, the simple percent agreement was in the range of 95.8% to 98.4%.

Gwet's Agreement Statistics Comparing Viral Suppression Definitions

The overall Gwet's AC1 score for the three viral suppression definitions showed an almost perfect agreement of 0.92 (0.83-1.00) for the total sample. When stratified by race/ethnic group, Haitians (AC1 = 0.87) and non-Hispanic Blacks (AC1 = 0.88) had the lowest agreement coefficients across all three definitions. The Gwet's scores between each pair of definitions also indicated almost perfect agreement; however, the pairwise analyses between maintained and sustained viral definitions demonstrated the highest levels of agreement (0.93 to 0.98) in the total sample and across racial/ethnic groups, as shown in Figure 2.

Positive and Negative Predictive Values

Using recent viral suppression definition as the reference standard, the PPVs for each of maintained and sustained viral suppression (as the diagnostic tests) for the total

sample were 100% while the NPVs were low at 62% (95% CI: 59.1, 64.9) for maintained and 53% (95% CI: 50.1, 55.6) for sustained viral suppression.

Associations of Viral Suppression Definitions with Clients' Characteristics

Across the three definitions, clients' characteristics significantly associated with not being viral suppressed were being non-Hispanic Black and Haitian (vs. non-Hispanic White/Other), younger age (being aged 18-24, 25-34 and 35-49 years [vs. 50 years]), having a household income of <100% of the FPL (vs. ≥200%), and an AIDS diagnosis in 2017 (Table 3). Differences in these magnitudes of association were observed, none of which were significant. For example, AORs for age group 18-24 years (vs. ≥50 years) had an absolute difference in magnitude of 0.05 or less and non-significant p-values for each of maintained (AOR: 0.34) and sustained viral suppression (AOR: 0.37) relative to recent viral suppression (AOR: 0.39).

Discussion

In this analysis of data of clients receiving care in the Miami-Dade County RWP, we observed significant variability in determining clients' viral suppression rates in 2017 depending on the definition used. Sustained viral suppression, that is, having consistent suppressed VL on all tests, was the most stringent definition and showed the least proportion of clients meeting this requirement. In contrast, the standard definition based on the most recent VL test in the year classified the most proportion of clients as suppressed, and this estimate (89.8%) was higher than the national average (85.9%) reported for RWP clients in 2017 (Health Resources and Services Administration, 2020). Recent viral suppression overestimated maintained and sustained viral suppression by 7.0% and 10.1%, respectively. Consistent with other studies (Crepaz et al., 2017; Marks et al., 2016), our findings suggest that we are understating the stability of clients to be virally suppressed across time if only considering last VL test. Given that the consensus

is to have a higher proportion of PWH virologically suppressed over time to avert HIV transmission and consequently, reduce HIV incidence (Chakraborty et al., 2017; Das et al., 2010; Henard et al., 2012; Montaner et al., 2010; Solomon et al., 2016), using the least stringent definition of recent viral suppression has some limitations. If the goal is to use viral suppression as a proxy to monitor treatment effectiveness and medication compliance over a given period, then using the standard definition of last VL test will systematically misclassify some groups of individuals as suppressed.

The study demonstrated substantial differences in the proportion of the viral suppression measures by race/ethnicity. Among the racial/ethnic groups, non-Hispanic Blacks and Haitians had greater relative differences than non-Hispanic Whites/Others and the total sample averages across all pairwise comparisons of viral suppression definitions. Hispanics had the highest suppression rates among the groups. Although the majority of clients in the analytic cohort had maintained and sustained viral suppression, proportions in non-Hispanic Blacks were lower than those reported in an assessment of national HIV surveillance data (Crepaz et al., 2017). When using agreement statistics, we found differences across all three definitions and between pairwise comparisons of the definitions. Non-Hispanic Blacks and Haitians had slightly less agreement between the definitions than non-Hispanic Whites/Others. Compared with non-Hispanic Whites/Others, non-Hispanic Blacks and Haitians had lower odds of viral suppression for all three definitions. which are largely influenced by the social determinants of health such as poverty level (Beer et al., 2016; Nwangwu-Ike et al., 2018), education (Beer et al., 2016; Nwangwu-Ike et al., 2018), and health insurance (Beer et al., 2016). These disparities may contribute to the differences in magnitudes of the measures of viral suppression definitions that disproportionately affect minority groups, particularly non-Hispanic Blacks and Haitians. Notably, we identified an inverse relationship between

household income levels and the relative differences in viral suppression definitions. Clients with lower household income levels had greater inter-definition differences in viral suppression, which markedly diminished in those in households with higher income. Moreover, the relative differences in the viral suppression definitions for clients who were not enrolled in the ACA were twice that for enrollees suggesting higher viral burden over time in the former group. Similarly, we found higher odds of being virally suppressed for ACA enrollees compared with non-enrollees for each definition. A possible explanation is that the ACA affords low-income and under-insured PWH broader access to medical treatment beyond those that target HIV, which may improve the likelihood of achieving viral suppression. Additionally, ACA-eligible clients are demographically different from non-ACA clients. Another explanation is that people with a household income less than 100% of FPL are ineligible for ACA.

We identified a dose-response relationship between age distribution, CD4 counts and the number of VL tests performed, and the relative differences in viral suppression definitions. With increasing age, the variations in the viral suppression measures narrowed substantially, implying that younger age groups performed worse when multiple measures of viral suppression were used compared with older groups. A national study found that, on average, younger age groups spent more time over a 2-year period in unsuppressed status than older age groups (Crepaz et al., 2016). Greater inter-definition differences were also observed in clients who had lower CD4 counts and more VL tests performed than their counterparts. Interestingly, in the multivariable analysis, clients with 4 VL tests (vs. 2 tests) during 2017 were significantly more likely to achieve recent viral suppression; conversely, we noticed that clients with 5 VL tests (vs. 2 tests) had lower odds of achieving maintained and sustained viral suppression. It is likely that a client's clinical status may influence the frequency of tests performed. One

possible reason may be that clients who had less frequent tests in the year were clinically stable at their initial test and unlikely to require regular monitoring, whereas clients with more tests may have had an initial unsuppressed test, requiring more frequent engagements with the health care system. Regardless of the frequency of VL testing, ignoring other VL tests by using a single measure would fail to capture the VL dynamics over time. A national study found that, on average, PWH in care who had not achieved consistent viral suppression spent 60% of a 2-year period with unsuppressed VL (>200 copies/mL) (Crepaz et al., 2016).

The simplicity of utilizing recent viral suppression as a cross-sectional metric favors its usability over multiple measures in monitoring service delivery outcomes and indicators of the impact of innovations in ART or other therapies in the RWP. Using multiple measures to characterize viral suppression is a complex and arduous task as it relies on collecting routine health data in clients who have sufficient engagement and retention in care. Notwithstanding, as noted earlier, if a program's goal is to use viral suppression to monitor the potential for ongoing transmission, or its focus is on treatment as prevention, then capturing fluctuations in VL that occur across time using cumulative measures may be better for enhanced monitoring. It may, therefore, be worthwhile to report estimates for different measures of viral suppression definitions to obtain a more nuanced description of the HIV epidemic. In the absence of this, maintained viral suppression may be a more useful measure given that it is less complicated to analyze, performs better than recent viral suppression and closer to sustained viral suppression in measuring viral burden. Additionally, unlike sustained viral suppression, maintained viral suppression is a better estimator of continuity of ART and retention in care. As an evaluation measurement for client care for agencies whose

"retention/stability" of clients is a subject of scrutiny, it is admittedly a whole lot better than recent viral suppression.

One limitation of our study is that our findings apply only to a subset of the population with HIV who are engaged in care in the RWP and therefore, may have limited generalizability to persons with HIV who reside in other US geographic regions. Regarding our analytic cohort comprising of clients with two or more VL tests, although we attempted to capture additional clients who had only one test in 2017 by including their last VL test in 2016, our criteria restricted us from including clients who had only one suppressed VL or no test throughout the period to ensure we had sufficient information to measure consistent viral suppression. This may have inadvertently impacted our findings. Although our data includes "date of first diagnosis" which could have been used as a proxy to measure the recency of HIV infection, we had a lot of missing data for this variable. Therefore, we were unable to accurately differentiate between newly infected clients and those with long-term HIV infection to define a well-representative sample. Given that studies have demonstrated markedly elevated VL during the acute stage of HIV infection (Fiebig et al., 2003; Pilcher et al., 2007), clients at the early stage of the disease may likely have high VL measures that would bias our estimates.

Conclusion

Our findings highlight the variability in the estimates of viral suppression definitions, particularly across race/ethnicity, age, socioeconomic and clinical status. To ensure optimal benefits for PWH and adequate monitoring of programmatic outcomes, it may be beneficial to report estimates using maintained or sustained viral suppression in addition to recent viral suppression.

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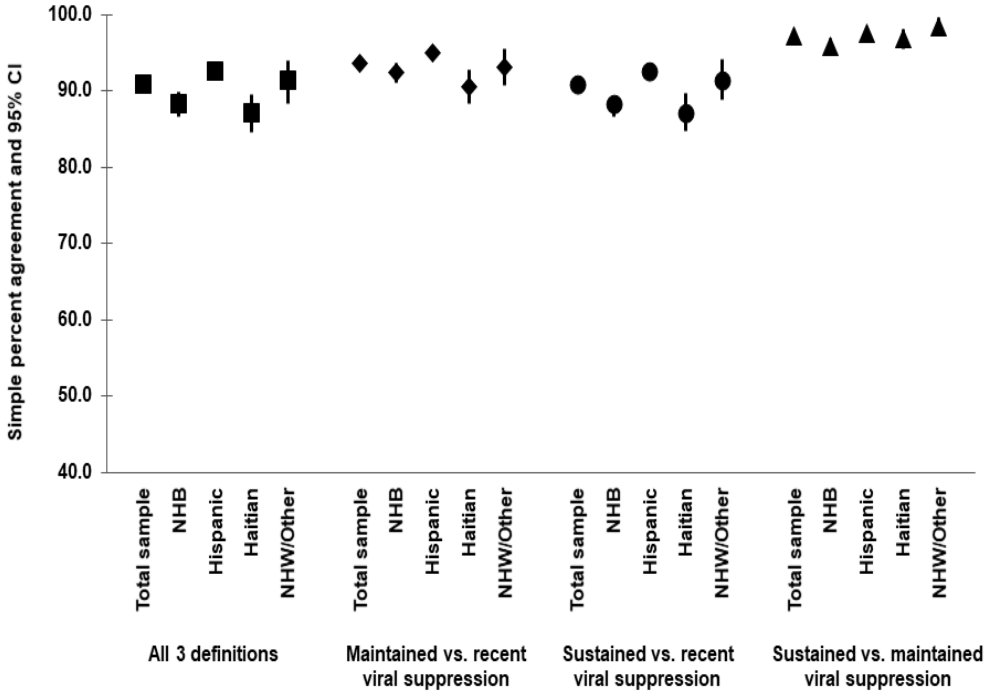

Figure 1. Simple percent agreement based on definitions of measures of viral suppression

Abbreviations: CI: confidence interval; NHB: non-Hispanic Black; NHW: non-Hispanic White

Total sample, n= 6503; non-Hispanic Black, n=1583; Hispanic, n=3777; Haitian, n=711; non-Hispanic White/Other, n=432

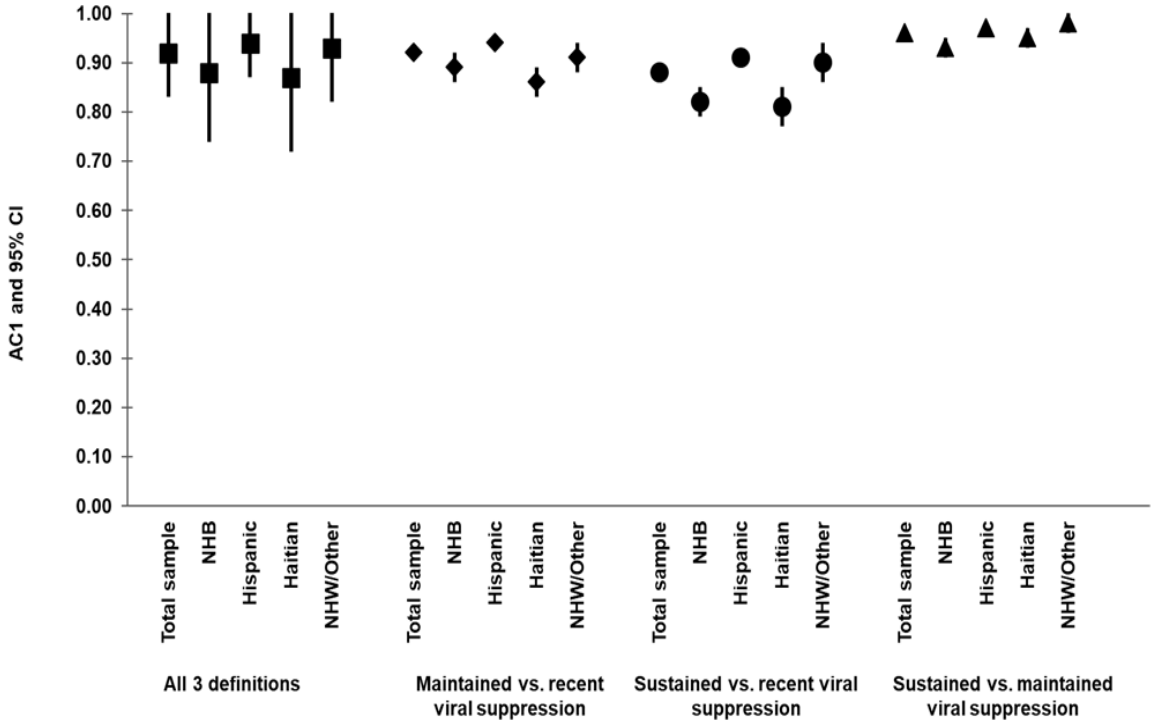

Figure 2. Gwet's agreement coefficient type 1 statistics based on definitions of measures of viral suppression

Abbreviations: AC1: Gwet's agreement coefficient type 1; CI: confidence interval; NHB: non-Hispanic Black; NHW: non-Hispanic White

Total sample, n= 6503; non-Hispanic Black, n=1583; Hispanic, n=3777; Haitian, n=711; non-Hispanic White/Other, n=432

Table 2. Estimates of positive and negative predictive values from pairwise comparisons between viral suppression definitions

Reference standard	*Diagnostic test*											
	Recent viral suppression				Maintained viral suppression				Sustained viral suppression			
	PPV	95% CI	NPV	95% CI	PPV	95% CI	NPV	95% CI	PPV	95% CI	NPV	95% CI
Recent viral suppression	--	--	--	--	100	--	62	59.1, 64.9	100	--	53	50.1, 55.6
Maintained viral suppression	93.0	92.4, 93.7	100	--	--	--	--	--	100	--	85	83.3, 87.3
Sustained viral suppression	89.8	89.1, 90.6	100	--	96.6	96.1, 97.1	100	--	--	--	--	--

Abbreviations: CI: confidence intervals; NPV: negative predictive value; PPV: positive predictive value

Table 3: Adjusted odds ratios for recent viral suppression versus cumulative measures of viral suppression for clients in the Miami-Dade Ryan White HIV/AIDS program, 2017 (n=6503)

	Recent viral suppression		Maintained viral suppression[a]		Sustained viral suppression[a]	
Characteristics	AOR	95% CI	AOR	95% CI	AOR	95% CI
Race/ethnicity						
Non-Hispanic Black	**0.49**	**0.33, 0.74**	**0.68**	**0.50, 0.93**	**0.62**	**0.46, 0.84**
Hispanic	0.86	0.56, 1.31	1.19	0.86, 1.64	1.04	0.76, 1.42
Haitian	**0.43**	**0.27, 0.70**	**0.60**	**0.41, 0.87**	**0.54**	**0.37, 0.77**
Non-Hispanic White/Other	ref		ref		ref	
Age group (years)						
18-24	**0.39**	**0.26, 0.58**	**0.34**	**0.24, 0.47**	**0.37**	**0.27, 0.51**
25-34	**0.35**	**0.27, 0.44**	**0.37**	**0.30, 0.45**	**0.40**	**0.33, 0.49**
35-49	**0.48**	**0.39, 0.59**	**0.52**	**0.44, 0.62**	**0.58**	**0.49, 0.67**
≥50	ref		ref		ref	
Sex						
Male	ref		--	--	--	--
Female	1.76	0.79, 3.88	--	--	--	--
Born in the United States						
Yes	**0.63**	**0.49, 0.81**	0.81	0.66, 1.00	**0.75**	**0.62, 0.92**
No	ref		ref		ref	
Household income (Percent of Federal Poverty Level)						
≥200%	ref		ref		ref	
100-199%	0.83	0.63, 1.08	**0.77**	**0.62, 0.96**	**0.72**	**0.59, 0.88**
<100%	**0.46**	**0.36, 0.59**	**0.43**	**0.35, 0.53**	**0.40**	**0.33, 0.49**

Enrollment in the Affordable Care Act						
Yes	**1.38**	**1.02, 1.87**	**1.49**	**1.17, 1.91**	**1.53**	**1.22, 1.93**
No	ref		ref		ref	
Initial HIV acquisition category						
Heterosexual contact						
Men	0.59	0.26, 1.34	0.93	0.76, 1.13	0.96	0.79, 1.16
Women	0.92	0.73, 1.17	0.85[b]	0.70, 1.03	0.84[c]	0.70, 1.01
MSM	ref		ref		ref	
IDU or IDU + MSM	0.61	0.31, 1.18	0.80	0.45, 1.42	0.79	0.46, 1.38
Other	**0.56**	**0.34, 0.93**	0.68	0.46, 1.01	**0.68**	**0.47, 0.99**
AIDS diagnosis in 2017						
Yes	**0.55**	**0.46, 0.66**	**0.55**	**0.47, 0.63**	**0.57**	**0.50, 0.66**
No	ref		ref		ref	
Number of VL results in 2017						
2	ref		ref		ref	
3	**1.73**	**1.43, 2.10**	1.14	0.98, 1.33	1.01	0.88, 1.18
4	**1.58**	**1.20, 2.07**	1.08	0.87, 1.34	0.83	0.68, 1.01
≥5	1.39	0.96, 2.01	**0.65[b]**	**0.49, 0.84**	**0.57[c]**	**0.44, 0.74**

Abbreviations: AOR: adjusted odds ratio; CI: confidence intervals; IDU: injection drug use; MSM: male-to-male sexual contact; VL: viral load
Bolded values represent significant estimates
[a]Sex was dropped from the full model
[b]p-value <0.05 for the z statistic to test whether there is a statistically significant difference in the log odds estimates obtained for the maintained viral suppression relative to recent viral suppression
[c]p-value <0.05 for the z statistic to test whether there is a statistically significant difference in the log odds estimates obtained for the sustained viral suppression relative to recent viral suppression

MANUSCRIPT 3

Person-time spent with HIV viral load above 1500 copies/mL among Miami-Dade County Ryan White Program clients, 2017-2019: A retrospective analysis

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Abstract

HIV transmission risk significantly increases at HIV viral load >1500 copies/mL. The objective of this study was to determine the percentage of person-time spent with viral load above 1500 copies/mL and the associations of demographic, clinical, and psychosocial factors, and this outcome among persons with HIV receiving care in Miami-Dade County. A retrospective analysis of data from clients enrolled in the Miami-Dade County Ryan White Program Part A and Minority AIDS Initiative (RWP) from 2017-2019 was performed. We computed person-time (in years) spent with viral load >1500 copies/mL in follow-up HIV care by utilizing consecutive viral load pairs and calculating the length of time between each pair and the corresponding time spent for the period of observation. Differences in demographic, clinical and psychosocial factors were assessed using Mann Whitney U and Kruskal Wallis tests. The association between person-years spent with viral load >1500 copies/mL and selected client characteristics were analyzed using a random-effects zero-inflated negative binomial model. Among the 6390 clients, 42% were aged 50 or older, 52% MSM, and 59% Hispanic. Overall, person-years with viral load >1500 copies/mL care was 7.5%. On average, clients spent 27.4 days per year at substantial risk of transmitting HIV. Percentage of person-years spent with viral load above 1500 copies/mL differed across demographic, clinical, and psychosocial factors. Younger age, AIDS diagnosis, and drug use in the preceding 12 months were all associated with longer time spent at viral load >1500 copies/mL. On average, persons with HIV spent nearly a month per year at substantial risk of

transmitting HIV. We identified client-level characteristics that impact person-time spent with viral load >1500 copies/mL, highlighting the specific HIV needs of some populations that require tailored interventions.

Introduction

Critical advances in HIV care and treatment services have preserved immune function (Smith et al., 2004) and reduced HIV transmission risk (Li et al., 2019) in persons with HIV (PWH) who are aware of their HIV infection, retained in care, and have achieved and maintained viral suppression. However, not all PWH have attained these milestones resulting in ongoing HIV transmissions and challenging efforts to reduce HIV incidence.

In Miami-Dade County, Florida, current policies, and programmatic efforts to eliminate HIV transmission are geared towards prioritizing screening, providing rapid access to treatment and ensuring retention in care, promoting pre-exposure prophylaxis, and increasing community engagement to achieve viral suppression (Florida Department of Health HIV/AIDS Section, 2020). Although these efforts have led to a slight decline in annual HIV diagnosis rates in recent years (42.9 cases per 100 000 in 2017 to 41.7 cases per 100 000 in 2019) (Florida Department of Health HIV/AIDS Section, 2020), Miami-Dade County still had over three times the national rate (13.2) and more than twice the rate of major cities such as New York City (17.7), San Francisco (15.8) and Washington, DC (15.7) in 2019 (Centers for Disease Control and Prevention, 2021). Among the individual- and structural-level barriers that limit the achievement of optimal treatment (Kalichman et al., 2021; Kimmel et al., 2018; Wohl et al., 2017), poor adherence and retention in care have the most impact on not achieving viral suppression (Mugavero, Amico, et al., 2012; Mugavero, Westfall, et al., 2012; Tarantino et al., 2020; Tripathi et al., 2011). A modeling study by the Centers for Disease Control and

Prevention (CDC) in 2015 estimated that diagnosed persons retained in care and those unretained in care accounted for 8.5% and 61.3% of new HIV transmissions in 2009, respectively (Skarbinski et al., 2015). In 2019, only 67% of PWH in Miami-Dade County were retained in care, and only 62% achieved viral suppression (Florida Department of Health HIV/AIDS Section, 2020), posing significant implications for transmission risk.

One major limitation of HIV studies is the use of a snapshot of a patient's viral load, typically the last viral load (≤200 copies/mL) of a given year, to measure viral suppression. Recently, researchers have incorporated frequent fluctuations in viral load in the longitudinal assessment of viral suppression (Crepaz et al., 2018; Marks et al., 2016). Others have included the proportion of time a person spent at a given viral load in analyses to allow for a more nuanced description of a patient's clinical status, particularly their risk of onward transmission of HIV over time (Crepaz et al., 2018; Lesko et al., 2018; Marks et al., 2015). One study found that the risk of transmitting HIV to others significantly increases at viral load >1500 copies/mL (Quinn et al., 2000). Moreover, experiencing longer time with viral load >1,500 copies/mL exacerbates HIV transmission risk (Crepaz et al., 2018).

Several studies have shown that some populations in particular may be at high risk of transmission (Hughes et al., 2018; Lesko et al., 2018; Marks et al., 2015; Mendoza et al., 2018; Olatosi et al., 2020). Indeed, the variability in HIV transmission dynamics observed between populations and individuals may be driven by several factors. Younger PWH (13-29 years), on average, spend more than half of the year with viral load >1,500 copies/mL (206 days) (Crepaz et al., 2020), relative to 136 days for older PWH (≥ 55 years) (Crepaz et al., 2018). Compared with Hispanics (172 days) and non-Hispanic Whites (149 days), non-Hispanic Blacks experienced longer mean time (190 days) during 2014 with viral load >1,500 copies/mL, suggesting racial disparities in

HIV transmission risk potential (Crepaz et al., 2018). Lower CD4+ count, homelessness, incarceration, and poor health insurance coverage may also be contributing to HIV transmission risk potential (Hughes et al., 2018; Mendoza et al., 2018). Given the multifaceted and complex drivers of HIV transmission risk, there is a need to expand the body of evidence beyond the little that is known. An in-depth understanding of transmission risk can provide foundational information about practical ways of achieving the objective of getting to zero transmissions. Therefore, we examined the percentage of person-time spent with viral load >1500 copies/mL and the association between demographic, clinical and psychosocial factors, and this outcome among PWH receiving care in Miami-Dade County.

Methods

Study design, data source and population

A retrospective analysis of anonymized data of clients enrolled in the Miami-Dade County Ryan White Program Part A and Minority AIDS Initiative (hereafter referred to as the RWP) collected from 2017-2019 was performed. During intake to the RWP, clients undergo a medical and county residency eligibility screening, and orientation process conducted by a medical case manager. In addition, financial eligibility is verified to ensure program funding is used as the payee of last resort. To determine each client's health-related and psychosocial service needs, health assessments are conducted at intake and twice a year by a medical case manager. Data for this study were sourced from the client intake, first 2017 health assessment and 2017-2019 laboratory files of the RWP and merged. Clients included in the analytic cohort were at least 18 years old, had undergone an intake process, and were deemed eligible for services in the RWP during 2017. Those with fewer than 2 viral load measurements during the study period or who

relocated or died or were missing an assessment during 2017 were excluded from the analysis.

Outcome variable

We computed person-time spent (in HIV care in years) with viral load >1500 copies/mL as described by Marks et al (Marks et al., 2015). For each client, we used all consecutive viral load pairs and calculated the length of time between each consecutive viral load pair and the corresponding person-time spent for the period of observation. For example, if the first viral load measurement of a client was on April 1, 2018, and a subsequent viral load measurement was November 27, 2018, the person-time observed was 240 days. If for the same client, there was another viral load measurement done before the end of the 36-month study period, and the former was 180 days apart from the latter, the total person-time calculated for the client was 420 days. We used the threshold that the viral load exceeded 1500 copies/mL to determine person-time spent >1500 copies/mL. When a consecutive pair of viral loads exceeded 1500 copies/mL, we assumed that the viral load throughout the person-time spent for the client for that period was greater than 1500 copies/mL. Alternatively, when the consecutive pair was equal to or less than 1500 copies/mL, then the viral load throughout the person-time spent for the client for that period was equal to or less than 1500 copies/mL. For a consecutive pair of viral loads where one measure was equal to or less than 1500 copies/mL and the other was greater than 1500 copies/mL, we estimated the person-time spent >1500 copies/mL. First, we computed the difference between the higher viral load and the threshold (1500), and the difference between the higher viral load and the lower viral load. Second, we calculated a fraction of these differences with the former as the numerator and the latter as the denominator. Then we multiplied this fraction by the person-time observed as explained earlier. For example, if the first viral load was 1000

copies/mL and the other was 3000 copies/mL, then the fraction will be (3000-1500)/(3000-1000) = 1500/2000 = 0.75. If the person-time observed was 240 days, then this client spent 0.75 x 240 days = 180 days with viral load >1500 copies/mL. To calculate the person-time spent in years, we divided by 365.25 days. Finally, we calculated the percentage person-time spent with viral load >1500 copies/mL for each client by summing person-time spent with viral load >1500 copies/mL for all consecutive pairs of viral loads and dividing by the total person-time spent for the period and multiplying by 100.

Predictors

Relevant demographic variables as reported in the client intake assessment were included. Age was categorized as “18-24 years,” “25-34 years,” “35-49 years,” and “≥50 years.” Race/ethnicity was grouped as Hispanic, non-Hispanic Black, Haitian, and non-Hispanic White/Other. “Other” accounted for 0.4% of the clients in care, and included Asians, Native American/Alaskan Natives, and Native Hawaiian/Pacific Islanders. Other variables included sex at birth (women, men) and US born status (“yes” if they were born in the U.S. and “no” for clients born in any of the U.S. territories or outside the U.S.). Initial mode of HIV acquisition (a self-reported account of how they contracted HIV) was grouped into heterosexual contact (men and women), men who had sex with men (MSM), injection drug use (IDU), and other, which included clients who were perinatally infected and those of undetermined status. Clients with both IDU and MSM exposures were included in the same risk category as those with IDU. Household income level (percent of Federal Poverty Level [FPL]), enrollment in an Affordable Care Act (ACA) health exchange plan, AIDS diagnosis (consistent with the CDC definition (Centers for Disease Control and Prevention, 2019)) in 2017 (diagnosed prior to or anytime during 2017) were also included. Psychosocial data were selected from the first comprehensive

health assessment conducted in 2017 guided by the Behavioral Model for Vulnerable Populations (Gelberg et al., 2000).

Analytical plan

Descriptive and exploratory analysis

All analyses were conducted in SAS/STATv14.2 (SAS Institute Inc, 2016). Descriptive analyses, including the proportion of person-time spent in care with viral load >1500 copies/mL, overall and by patient characteristics were computed. Differences in percentage person-time spent with viral load >1500 copies/mL for each stratification variable were compared using Mann Whitney U and Kruskal Wallis tests as appropriate in univariate analyses. Independent variables were checked for multicollinearity. We dropped sex at birth from further analyses because it was found to be highly correlated with HIV transmission risk category (r = -0.7305). HIV transmission category was the preferred choice because it depended on information from the sex at birth variable.

Model fit and selection

To evaluate the association between patient characteristics and person-time spent with a viral load >1500 copies/mL, we considered four theoretically possible Poisson family models given that it is more appropriate to analyze the rate of event occurrences, such as the time spent with viral loads at different intervals, than absolute counts. We included a random effects term in each model to account for correlated outcomes within clients. We conducted the analyses using the SAS nonlinear mixed model procedure (PROC NLMIXED). First, assuming equal mean and variance, we fitted a standard Poisson model to the data. Second, we fitted a negative-binomial (NB) model to account for any violation of the equidispersion assumption, particularly the large variability observed (Cameron & Trivedi, 2013), which may lead to overinflation of standard errors increasing the type I error rate (Potts & Elith, 2006). Given the likelihood

of a larger number of zero counts in the data observed than what is typically expected (i.e., a high proportion of clients demonstrating zero percentage person-time spent at viral load >1500 copies/mL), we considered zero-inflated distributions. Zero-inflated models assume that the zeros originate from a mixture of two processes: (i) true zeros - clients who are suppressed and unlikely to spend any time with viral load >1500 copies/mL, or (ii) random zeros - clients who may have had viral loads >1500 copies/mL and spent time at this threshold, but their viral loads were not captured during this period. Accordingly, the processes were represented by two components: the first predicts the true zero-only count (logistic component predicts whether the client spent "zero" person-time (years) with viral load >1500 copies/mL), and the second predicts both positive counts and the random zeros using an ordinary count distribution (Poisson or NB component predicts the likelihood of belonging to the higher end of the count distribution of person-time spent with viral load >1500 copies/mL). The two components are combined to calculate the probabilities of the outcome. As such, we fitted two-component mixture models, the zero-inflated Poisson (ZIP) and zero-inflated NB (ZINB) models to the data.

For each model, the SAS output produced four model fit indices: the likelihood value statistic (-2LL), the Akaike Information Criterion (AIC), the finite sample corrected AIC (AICC) and the Bayesian Information Criterion (BIC). The smaller the value of the indices, the closer the model fits the observed data. Finally, we selected the most parsimonious model based on these standard model selection criteria. In addition, we computed the overdispersion parameters for the NB and ZINB models and their corresponding p-values. This study was approved by the Florida International University Institutional Review Board.

Results

Characteristics of the cohort

The majority of the 6390 clients included in this analysis were MSM (52%) and Hispanic (59%). Forty-two percent of the cohort were aged 50 or older, 63% foreign-born, 76% had household income <200% of the FPL, and 85% were enrolled in an ACA health exchange plan. At enrollment, median CD4 count was 629 cells/μL (interquartile range [IQR]: 446, 882), and about 9% had a baseline viral load above 1500 copies/mL. Clients had a median of 7 (IQR: 5, 9) viral load measurements taken at a median of 117 days apart (IQR: 85, 161), and the median duration of observation (which corresponds to the length of time between the first and last viral load measurements) was 2.2 years (IQR: 1.6, 2.4).

Person-years spent in follow-up HIV care above 1500 copies/mL

The cohort contributed a total of 12,231.7 person-years in HIV care from 2017-2019. Of these, 915.7 (7.5%) were spent with viral load >1500 copies/mL. On average, the person-time spent with viral load >1500 copies/mL equates to an average of 27.4 days per year (0.075 x 365.25 days) per person. Subgroups with the highest proportions of person-years spent above the threshold were: age 18-24 years (13.3%), non-Hispanic Black (13.3%), having a household income lower than 100% of FPL (11.7%), and living with three or more minors in a household (11.3%). Similarly, clients who spent more than 15% of the time above 1500 copies/mL (i.e., over twice the overall percentage for the cohort) had fewer viral load measurements (15.2%), reported drug use in the preceding 12 months (20.9%), alcohol/drugs affected their adherence (15.3%), problems as a result of drug/alcohol use (31.1%), a need for substance use treatment (28.0%), being homeless (22.5%), legal needs (15.8%), and lack of needed food (17.8%).

In the univariate analyses, we found significant differences between all groups by person-years spent in HIV care with VL >1500 copies/mL except for clients who had a disability that prevented working compared with their counterparts as shown in Table 1.

Model comparison

The overdispersion parameters for both NB and ZINB were significant (8.60, p <.0001; and 0.11, p <.0001, respectively), indicating that NB is superior to Poisson and ZINB is superior to ZIP. Comparing the four models together, the three information criteria (AIC, AICC and BIC) illustrate a notable reduction in these indices for ZINB and the poorest fit for the Poisson model as represented in Table 2. The order of the goodness of fit among the four models was: ZINB, ZIP, NB, and Poisson, respectively. ZINB and ZIP were close, but ZINB offered a better fit. Even when ZINB and ZIP were further compared using the difference in −2LL, the result was significant (44477–42251 = 2,226, df = 12, p <.00001), favoring the more parsimonious ZINB model.

Probability of zero person-years with a viral load >1500 copies/mL (ZINB model, logistic component)

As earlier stated, the logistic component predicts the probability of zero person-years vs. at least some person-years with viral load >1500 copies/mL. As such, compared with clients 50 years or older, the odds of zero person-years spent with viral load >1500 copies/mL were lower in those aged 35-49 (adjusted odds ratio [AOR]: 0.62; 95% confidence interval [CI]: 0.50, 0.77), 25-34 (AOR: 0.45; 95% CI: 0.34, 0.58) and 18-24 years (AOR: 0.43; 95% CI: 0.28, 0.68), conditional on random effects. Hispanics had higher odds of having zero person-years with viral load >1500 copies/mL relative to non-Hispanic Whites/Others (AOR: 2.73; 95% CI: 2.73; 1.84, 4.06), clients with household income ≥200% FPL (AOR: 3.29; 95% CI: 2.48, 4.35) and 100-199% FPL (AOR: 2.21; 95% CI: 1.77, 2.76) compared with <100% FPL, and those enrolled in an ACA health

exchange plan (AOR: 2.33; 95% CI: 1.73, 3.15). Holding all other factors constant, clients who had an AIDS diagnosis (0.54; 0.45, 0.65), reported alcohol (0.72; 0.54, 0.96) and drug use (0.44; 0.25, 0.78) in the last 12 months, received or needed mental health services (0.71; 0.55, 0.93), and were homeless (0.40; 0.27, 0.58) had lower odds of zero person-years above the threshold (Table 3). The significant random effect (5.22; p <.0001) showed considerable heterogeneity among clients with respect to the person-time spent above the threshold.

Rates of person-years spent above 1500 copies/mL (ZINB model, negative binomial component)

Higher rates of person-years spent above the threshold were observed for clients aged 25-34 (adjusted rate ratio [ARR]: 1.06; 95% CI: 1.01, 1.10) and 35-49 years (ARR: 1.05; 95% CI: 1.02, 1.09) compared with 50 years or older, those with an AIDS diagnosis (1.09; 1.05, 1.13) and those who reported drug use in the preceding 12 months (1.09; 1.01, 1.18). Whereas we found lower rates of person-years above the threshold in clients with a household income of 100-199% of FPL (0.95; 0.92, 0.99) compared to those below 100% of FPL. The random effect for this component was not statistically significant (p = 0.9705), indicating lack of heterogeneity among clients (Table 3).

Discussion

In this analysis of a large, diverse cohort of adult PWH in Miami-Dade County, we observed that person-time spent (in years) in follow-up HIV care was 7.5%. On average, PWH in care spent 27.4 days per year with substantial HIV transmission risk. Percentage of person-years spent with viral load above 1500 copies/mL differed across demographic, socioeconomic, clinical, and psychosocial factors. Younger age, AIDS diagnosis and drug use in the preceding 12 months were all associated with longer time spent with viral load >1500 copies/mL.

Our major finding of 7.5% of person-years spent with viral load >1500 copies/mL among PWH in care was consistent with a study conducted among PWH highly engaged in care in San Francisco (7.4%) (Hughes et al., 2018). In contrast, some earlier studies have reported higher rates of person-time spent above 1500 copies/mL. Patients receiving care at Johns Hopkins HIV Clinic (2010-2015) spent 14.8% of person-years with viral load >1500 copies/mL (Lesko et al., 2018). In a longitudinal study of PWH receiving care in HIV specialty clinics in the U.S. (2000-2014), person-time spent above 1500 copies/mL was 16.4% (Mendoza et al., 2018). Another study examining person-time spent above 1500 copies/mL among newly diagnosed PWH engaged in care using the South Carolina HIV surveillance data (2014-2017) reported 18.0% (Olatosi et al., 2020). Patients in care at six HIV clinics in the U.S. (2009-2013) spent 26.3% at increased risk of transmitting HIV during follow-up HIV care (Marks et al., 2015). An analysis of the National HIV Surveillance System in 2014 found that PWH in care spent 48.3% of their time with a viral load >1500 copies/ml, although only individuals who did not achieve sustained viral suppression were included (Crepaz et al., 2018). One possible reason for this low percentage found in our study could be the comprehensive medical and support services provided by the RWP to PWH (Health Resources and Services Administration, 2020), many of whom report psychosocial problems (Bravo et al., 2010), lack health insurance coverage or face coverage limits (Bradley et al., 2016), or confront cost (Wohl et al., 2017) and transportation barriers to care (Dandachi et al., 2019; Sagrestano et al., 2014; Ward et al., 2021). The RWP services are specifically designed to address these barriers and improve health outcomes (Health Resources and Services Administration, 2020). For example, in Miami-Dade County, RWP services are often co-located thereby reducing complexities with regards to seeking additional specialty care and transportation barriers that have been found to be associated with

lack of viral suppression (Goswami et al., 2016). Notably, continued efforts are being made to further drive the recent declines in annual HIV diagnosis rates in the county. In 2017, the RWP in partnership with the Florida Department of Health in Miami-Dade County, key agencies and other stakeholders developed the “Getting to Zero” Taskforce Recommendations (Miami-Dade HIV/AIDS Partnership, 2017). These recommendations provide guidance for implementing innovative, tailored, and sustained population-wide evidence-based HIV prevention and treatment strategies, including systems change in a predominantly racial/ethnic minority setting (Miami-Dade HIV/AIDS Partnership, 2017). Even though weaknesses and challenges remain in the HIV care system, these strategies are continuously refined to meet the specific HIV needs of the Miami-Dade community (Health Council of South Florida & Florida Department of Health in Miami-Dade County, 2020; *Miami-Dade County “Getting to Zero” HIV/AIDS Task Force Implementation Report 2017-2018*, n.d.). In 2020, in line with the Ending the HIV Epidemic (EHE) initiative in the U.S., the EHE in Miami-Dade County project was launched to further address the significantly high HIV transmission rates in the community.(Health Council of South Florida & Florida Department of Health in Miami-Dade County, 2020) Four key strategies, referred to as foundation pillars, were adopted: diagnose, treat, prevent, and respond (Health Council of South Florida & Florida Department of Health in Miami-Dade County, 2020). As EHE initiatives are implemented, it is expected that Miami-Dade would get closer to meeting its goals of achieving zero transmissions.

Although the trend in age disparities in HIV outcomes have narrowed in recent years (Mandsager et al., 2018), it is not surprising that we found that young adults were more likely to spend longer time with viral loads above 1500 copies/mL. This is consistent with other studies (Crepaz et al., 2018, 2020; Marks et al., 2015). The period

of health care transition from adolescent- to adult-centered care represents one of the most vulnerable points for young PWH. During this period, interruptions in and disengagement from care are common leading to poor retention in care and lack of viral suppression (Hussen et al., 2017; Ryscavage et al., 2016). Additionally, young adults experience perceived stigma, disclosure concerns, and adherence problems related to navigating and distrust in the health care system (Dobroszycki et al., 2017; Kahana et al., 2016; Zanoni & Mayer, 2014). Some authors have called for moving HIV services beyond medical sites and engaging young adults using mobile technologies (Arayasirikul et al., 2020; Rotheram-Borus, Lee, et al., 2018) given the widescale ownership, adoption, and utilization of advanced technology in this population (Rotheram-Borus, Davis, et al., 2018). Incorporating innovative mobile health technology and social media in HIV care has shown some promise (Arayasirikul et al., 2020; Badawy et al., 2017; Brooks et al., 2020; Tanner et al., 2018) and may offer an opportunity to rapidly reach and scale prevention and treatment programs in this population. For example, a recent single-arm efficacy trial compared pre- and post-implementation of a digital HIV care navigation among young PWH in San Francisco found increased odds of viral suppression at 6 months following the intervention (Arayasirikul et al., 2020).

When evaluating the psychosocial factors, we found that reporting alcohol use, drug use, and homelessness were associated with a decreased odds of zero-years spent with viral load above 1500 copies/mL. One study also found a similar relationship between homelessness and time spent with viral load >1500 copies/mL (Hughes et al., 2018). Other studies have reported findings for alcohol, drug use and homelessness for PWH in the Ryan White Program (Irvine et al., 2017; M. J. Li et al., 2020), although with a more stringent threshold of unsuppressed viral load at >200 copies/mL. Substance use, including alcohol and drug use, impedes medication adherence, stimulates more

rapid disease progression, and drives sexual transmission of HIV (Carrico, 2011; Hendershot et al., 2009; Mellins et al., 2009). However, substance use is amenable to effective substance abuse treatment and support services that have been shown to reduce alcohol and drug use, and HIV transmission (Metzger et al., 2010; Volkow et al., 2011). Policies and programs designed to increase access to these services for PWH remain a high priority.

We observed some interesting findings that may be relevant to clinical practice. In a secondary analysis, we assessed whether the frequency of viral load measurements and having a higher percentage of viral load pairs with intervals longer than 6 months were associated with longer time spent with viral load >1500. Clients with fewer viral load measurements had longer periods with viral load >1500 relative to those with more measurements (2-5: 15.2%; 6-10: 5.6%; >10 tests: 5.9%, p<.0001). In addition, we found that as the percentage of interval time over 6 months increased, clients spent longer periods with viral load >1500 (<10%: 4.8%; 10-25%: 8.3%; >25%: 9.8%, p <.0107). A study across six clinics in the U.S. found twice the rates for person-time spent at viral load >1500 copies for patients in HIV care with 25% of their viral load pairs exceeding a 6-month interval compared with those having fewer than 10% (Marks et al., 2015). We, therefore, speculate that a more aggressive treatment strategy that incorporates frequent viral load measurements at shorter intervals may reduce person-time spent above the threshold and decrease transmission risk.

We highlight several limitations in our study. First, we included only clients with 2 or more viral load measurements to calculate person-time spent with viral load >1500 copies/mL. If we assumed those with only 1 viral load dropped out of care, then these individuals were more likely to have had viral loads above 1500 copies/mL. This may have led to selection bias and an underestimate of the percentage of person-time spent

with viral load >1500 copies/ml among all RWP clients. Second, although our assessment of the psychosocial factors relied on information collected using non-standardized reporting instruments, which are subject to bias, we were able to explore these factors to provide preliminary evidence for further studies. This level of information is not typically available in HIV surveillance data. Third, even though we attempted to capture multiple viral loads to account for viral blips that may occur over time, it is not feasible to fully account for each client's complete viral load status throughout the observation period. Finally, researchers have argued for a need to address the impact of structural-level factors on HIV outcomes given their contributions to disparities among disadvantaged populations (Kahana et al., 2016; Raymond et al., 2014). Our study did not explore the role of neighborhood-level variables on time spent above 1500 copies/mL; this is an area for future research.

Conclusion

Identification of patient-level characteristics that impact person-time spent with viral load >1500 copies/mL is an essential step in optimizing HIV care to eliminate HIV transmission risk. Continued efforts to meet the specific HIV needs of underserved populations must be supported by all key players to fulfill the goals of the EHE initiative. Future research on undiagnosed and diagnosed PWH not retained in care is warranted to better understand their role in the HIV transmission dynamics.

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Table 1: Summary of the distribution of person-time (years) in follow-up HIV care and viral load above 1500 copies/mL among Ryan White Program clients during 2017-2019 (N= 6390)

	N	Person-years in follow-up HIV care n	Person-years in follow-up HIV care with VL >1500 copies/mL n (% of person-years)	p-value*
All participants	6390	12231.7	915.7 (7.5)	
Age group (years)				<.0001
18-24	257	474.9	63.1 (13.3)	
25-34	1132	2112.2	224.4 (10.6)	
35-49	2281	4479.5	366.8 (8.2)	
50+	2715	5153.7	261.4 (5.1)	
Missing	5			
Race/ethnicity				<.0001
Non-Hispanic Black	1526	2650.4	351.6 (13.3)	
Hispanic	3741	7435.0	402.4 (5.4)	
Haitian	695	1359.1	117.6 (8.7)	
Non-Hispanic White/Other	428	787.2	44.1 (5.6)	
Sex at birth				
Men	4897	9450.17	684.20 (7.2)	<.0003
Women	1493	2781.55	231.54 (8.3)	
Household income (Percent of Federal Poverty Level)				<.0001
≥200%	1503	2996.9	109.3 (3.6)	
100-199%	2262	4509.2	253.5 (5.6)	
<100%	2625	4725.6	553.0 (11.7)	

US born				<.0001
Yes	2028	3533.7	428.7 (12.1)	
No	4362	8698.0	487.0 (5.6)	
HIV transmission risk category				<.0001
Male with heterosexual contact	1427	2669.2	214.9 (8.1)	
Female with heterosexual contact	1410	2603.0	265.9 (10.2)	
MSM	3315	6539.5	386.9 (5.9)	
IDU or IDU + MSM	81	136.6	11.4 (8.4)	
Other	157	283.4	36.6 (12.9)	
Enrolled in the Affordable Care Act health insurance exchange				<.0001
Yes	961	2004.1	51.3 (2.6)	
No	5429	10227.6	864.4 (8.5)	
Diagnosis of AIDS (history)				<.0001
Yes	2613	4914.5	499.6 (10.2)	
No	3777	7317.2	416.2 (5.7)	
Alcohol use in the last 12 months				
Yes	716	1270.2	178.2 (14.0)	<.0001
No	5674	10961.5	737.6 (6.7)	
Drug use in the last 12 months				
Yes	447	745.4	156.0 (20.9)	<.0001
No	5943	11486.3	759.7 (6.6)	

Alcohol/drugs affect adherence				<.0001
Yes	297	527.7	80.6 (15.3)	
No	6093	11704.1	835.1 (7.1)	
Feeling depressed or anxious				<.0001
Yes	926	1655.2	222.7 (13.5)	
No	5462	10573.5	693.1 (6.6)	
Missing	2			
Having difficulty sleeping				<.0001
Yes	697	1232.2	172.4 (14.0)	
No	5691	10996.4	743.3 (6.8)	
Missing	2			
Receives or needs mental health services				<.0001
Yes	971	1705.4	223.7 (13.1)	
No	5413	10519.7	690.9 (6.6)	
Missing	6			
Drug/alcohol use resulted in problems with daily activities/legal issue/hazardous situation				<.0001
Yes	130	193.2	60.0 (31.1)	
No	6260	12038.5	855.7 (7.1)	
Would like substance use treatment now				<.0001
Yes	82	114.8	32.2 (28.0)	
No	6308	12116.9	883.6 (7.3)	

Homeless				<.0001
Yes	309	500.6	112.9 (22.5)	
No	6081	11731.1	802.9 (6.8)	
Any legal needs				<.0001
Yes	101	166.4	26.3 (15.8)	
No	6289	12065.4	889.4 (7.4)	
Household size				0.0003
One	5070	9690.4	764.6 (7.9)	
Two	809	1569.9	75.2 (4.8)	
Three	289	549.3	43.4 (7.9)	
Four or more	222	422.2	32.5 (7.7)	
Number of minors in household				0.0026
None	5723	10968.1	802.6 (7.3)	
One	394	745.0	67.1 (9.0)	
Two	191	370.1	29.2 (7.9)	
Three or more	82	148.6	16.8 (11.3)	
Lives with minor only				0.0002
Yes	229	417.7	48.2 (11.5)	
No	6161	11814.0	867.5 (7.3)	
Disability that prevents working				0.6045
Yes	922	1419.6	124.0 (8.7)	
No	5468	10812.1	791.7 (7.3)	
Unemployed				<.0001
Yes	2430	4206.4 (34.4)	468.5 (11.1)	

No	3960	8025.4 (65.6)	447.3 (5.6)	
Client not getting food they need				<.0001
Yes	97	162.6	28.9 (17.8)	
No	6293	12069.1	886.8 (7.3)	

*p-values represent Mann Whitney U and Kruskal Wallis tests as appropriate
IDU: injection drug use; MSM: men who have sex with men

Table 2. Model fit statistics

Random-intercept model	-2 LL	AIC	AICC	BIC	k
Poisson	324011	324083	324083	324326	--
Negative binomial	51703	51777	51777	52027	8.60*
Zero-inflated Poisson	44477	44621	44621	45107	--
Zero-inflated negative binomial	42251	42397	42397	42890	0.11*

Abbreviations: −2LL: likelihood value statistic; AIC: Akaike Information Criterion; AICC: the finite sample corrected AIC; BIC: Bayesian Information Criterion; k: overdispersion parameter

*p-value <.0001

Table 3: Estimates of the zero-inflated and negative binomial parts of the random-intercept ZINB model for factors associated with percentage person-time spent with viral load >1500 copies/mL

	Logistic Zero person-years with viral load >1500 copies/mL				Negative binomial Person-years with viral load >1500 copies/mL			
Variables	**Adjusted Odds Ratio**	**95% CI**		**p-value**	**Adjusted Rate Ratio**	**95% CI**		**p-value**
Age group (years)								
18-24	**0.43**	**0.28**	**0.68**	**0.0003**	0.99	0.92	1.06	0.7282
25-34	**0.45**	**0.34**	**0.58**	**<.0001**	**1.06**	**1.01**	**1.10**	**0.0079**
35-49	**0.62**	**0.50**	**0.77**	**<.0001**	**1.05**	**1.02**	**1.09**	**0.0032**
50+	Ref				Ref			
Race/ethnicity								
Non-Hispanic Black	0.97	0.65	1.43	0.8747	1.01	0.94	1.08	0.8686
Hispanic	**2.73**	**1.84**	**4.06**	**<.0001**	1.04	0.96	1.12	0.3095
Haitian	1.07	0.66	1.73	0.7778	1.01	0.92	1.10	0.8301
Non-Hispanic White/Other	Ref				Ref			
Household income (Percent of Federal Poverty Level)								
≥200%	**3.29**	**2.48**	**4.35**	**<.0001**	0.98	0.93	1.02	0.3206
100-199%	**2.21**	**1.77**	**2.76**	**<.0001**	**0.95**	**0.92**	**0.99**	**0.0205**
<100%	Ref				Ref			
US born								
Yes	1.05	0.80	1.39	0.7215	1.04	0.99	1.09	0.1446
No	Ref				Ref			
HIV transmission risk category								
Heterosexual male	1.20	0.91	1.59	0.1920	0.97	0.93	1.01	0.1605
Heterosexual female	0.78	0.61	1.01	0.0561	1.02	0.98	1.06	0.3023

MSM	Ref				Ref			
IDU or IDU + MSM	1.03	0.47	2.25	0.9332	0.90	0.80	1.02	0.1067
Other	0.80	0.46	1.41	0.4488	0.94	0.88	1.02	0.1381
Enrolled in the Affordable Care Act health insurance exchange								
Yes	**2.33**	**1.73**	**3.15**	**<.0001**	0.99	0.94	1.05	0.7539
No	Ref				Ref			
Diagnosis of AIDS (history)								
Yes	**0.54**	**0.45**	**0.65**	**<.0001**	**1.09**	**1.05**	**1.13**	**<.0001**
No	Ref				Ref			
Alcohol use in the last 12 months								
Yes	**0.72**	**0.54**	**0.96**	**0.0248**	0.99	0.95	1.03	0.6254
No	Ref				Ref			
Drug use in the last 12 months								
Yes	**0.44**	**0.25**	**0.78**	**0.0053**	**1.09**	**1.01**	**1.18**	**0.0340**
No	Ref				Ref			
Alcohol/drugs affect adherence								
Yes	1.61	0.87	2.97	0.1276	0.98	0.91	1.04	0.4733
No	Ref				Ref			

Feeling depressed or anxious								
Yes	0.76	0.55	1.06	0.1118	1.03	0.98	1.08	0.2430
No	Ref				Ref			
Having difficulty sleeping								
Yes	0.73	0.52	1.04	0.0844	1.00	0.95	1.05	0.9759
No	Ref				Ref			
Receives or needs mental health services								
Yes	**0.71**	**0.55**	**0.93**	**0.0132**	0.99	0.95	1.02	0.4228
No	Ref				Ref			
Drug/alcohol use resulted in problems with daily activities/legal issue/hazardous situation								
Yes	0.53	0.28	1.03	0.0600	0.97	0.91	1.04	0.4047
No	Ref				Ref			
Would like substance use treatment now								
Yes	0.93	0.44	1.95	0.8475	1.04	0.96	1.12	0.3455
No	Ref				Ref			
Homeless								
Yes	**0.40**	**0.27**	**0.58**	**<.0001**	1.03	0.99	1.08	0.1431
No	Ref				Ref			
Any legal needs								
Yes	0.83	0.43	1.59	0.5805	0.96	0.89	1.04	0.3404
No	Ref				Ref			

Household size								
One	Ref				Ref			
Two	**1.69**	**1.24**	**2.29**	**0.0009**	1.00	0.95	1.06	0.9784
Three	0.97	0.61	1.56	0.9059	0.97	0.90	1.05	0.4468
Four or more	1.21	0.66	2.21	0.5405	1.03	0.93	1.13	0.5781
Number of minors in household								
None	Ref				Ref			
One	0.77	0.51	1.18	0.2383	1.02	0.96	1.09	0.5163
Two	1.26	0.66	2.41	0.4912	1.08	0.96	1.20	0.1956
Three or more	0.95	0.39	2.32	0.9130	1.01	0.88	1.17	0.8613
Lives with minor only								
Yes	0.59	0.34	1.04	0.0686	0.99	0.90	1.08	0.7615
No	Ref				Ref			
Unemployed								
Yes	1.02	0.82	1.27	0.8563	1.01	0.98	1.05	0.3712
No	Ref				Ref			
Client not getting food they need								
Yes	0.63	0.33	1.20	0.1587	0.97	0.89	1.06	0.5353
No	Ref				Ref			
σ^2 intercept	**5.22**[a]	**4.81**	**5.63**	**<.0001**	0.000504[b]	-0.0263	0.02725	0.9705
k[c]	--	--	--	--	**0.1138**	**0.08752**	**0.14**	**<.0001**

[a]Random intercept term for the logistic component
[b]Random intercept term for the negative binomial component
[c]k is the dispersion parameter
Abbreviations: IDU: injection drug use; MSM: men who have sex with men. Bolded values represent significant p-values

CONCLUSION

The objective of this dissertation was to examine factors associated with HIV transmission risk potential for persons with HIV (PWH) using measures of time from HIV infection to diagnosis and trajectories of viral load suppression. Additionally, this dissertation sought to determine whether a single yearly viral load measure—the current standard to track the HIV epidemic in the United States—is reliable in assessing viral suppression for PWH. To address this objective, we used a CD4 depletion model and Cox regression analysis to assess the individual- and neighborhood-level factors associated with length of time from HIV infection to diagnosis for PWH in Florida during 2014-2018 as well as a random-effects zero-inflated negative binomial model to determine factors associated with experiencing longer time with viral load >1500 copies/mL from 2017-2019. In addition, we used Gwet's agreement statistics to examine variations in viral suppression definitions and agreement between each definition among clients in the Miami-Dade County Ryan White Program.

For our first aim, we hypothesized that longer median time between HIV infection and diagnosis will be observed among racial/ethnic minorities compared with non-Hispanic White, older adults compared with younger adults, and residing in a neighborhood with worse socioeconomic factors. Like earlier studies (Crepaz et al., 2021; Dailey et al., 2017; Hall et al., 2015; Robertson et al., 2020), we observed older adults had longer time to diagnosis that younger adults. Therefore, it was not surprising that we observed these findings. Because older people have lived longer, it is unlikely that younger people, especially those in the lowest age categories, have been infected longer. Despite the fact that non-Hispanic Blacks are more likely to undergo HIV testing compared with Whites (Gaines et al., 2016; Lo et al., 2018), we found longer median time to diagnosis for non-Hispanic Blacks than non-Hispanic Whites in our study. In line

with prior studies, our study suggests that neighborhood-level social determinants of health may play a role in this association (Cope et al., 2020; Joy et al., 2008; McDavid Harrison et al., 2008; Wiewel et al., 2017). We found that residing in a census tract with low education, high rates of rented housing and low household income were associated with longer time to diagnosis. Neighborhood-level poverty deprives people of critical resources such as education, economic opportunities, housing, and healthcare (Diez Roux, 2001), which may negatively impact their health-seeking behavior. Our findings suggest racial disparities in late HIV diagnosis and future areas for HIV preventive research, particularly among older adults and non-Hispanic Blacks. Novel strategies to increase access to HIV testing, particularly in the hard-to-reach population may help close the gaps in early diagnosis of HIV for older adults, racial/ethnic minorities, and disadvantaged populations. Enacting policies aimed at enhancing education, housing and employment may contribute to economic growth in resource-poor neighborhoods, thus alleviating poverty-related inequities.

For our second aim, we hypothesized that using a single viral load measure will overestimate maintained and sustained viral suppression by a greater degree for racial/ethnic minorities than for non-Hispanic Whites. We found that using a single measure of recent viral suppression overestimated maintained and sustained viral suppression measures by 7.0% and 10.1%, respectively. We also found significant relative differences in viral suppression definitions by race/ethnicity. Overall, non-Hispanic Blacks and Haitians had lower agreement scores than non-Hispanic Whites/Others across all three definitions, indicating greater variation in these definitions for these racial/ethnic minority populations. Previous studies have shown racial/ethnic disparities in viral burden (Beer et al., 2016; Bradley et al., 2016; Nwangwu-Ike et al., 2018), which are largely influenced by the social determinants of health such as poverty

level (Beer et al., 2016; Nwangwu-Ike et al., 2018), education (Beer et al., 2016; Nwangwu-Ike et al., 2018), and health insurance (Beer et al., 2016). These disparities may contribute to the differences in magnitudes of the measures of viral suppression definitions that disproportionately affect minority groups, particularly non-Hispanic Blacks and Haitians. It may, therefore, be worthwhile to report estimates for different measures of viral suppression definitions to obtain a more nuanced description of the HIV epidemic to ensure optimal benefits for underserved populations.

Finally, for our third aim, we hypothesized that racial/ethnic minorities compared with non-Hispanic Whites and younger adults compared with older adults will spend a longer time with viral load >1500 copies/mL. We found that the percentage of person-years spent with viral load above 1500 copies/mL differed across age and racial/ethnic groups. In our adjusted analysis, younger age was associated with longer time spent at viral load >1500 copies/mL, whereas race/ethnicity was not. While age disparities in HIV outcomes have diminished in recent years (Mandsager et al., 2018), it is not surprising that we found that young adults were more likely to spend longer time with viral loads above 1500 copies/mL. This is consistent with other studies (Crepaz et al., 2018, 2020; Marks et al., 2015). The transition from adolescent to adult-centered care is one of the most critical times for young PWH. Interruptions and disengagement from treatment are typical throughout this period, resulting in poor retention and viral suppression (Hussen et al., 2017; Ryscavage et al., 2016). Distrust in the health care system also plays a major role in adherence for young individuals (Dobroszycki et al., 2017; Kahana et al., 2016; Zanoni & Mayer, 2014). Using mobile technology for HIV services for young adults have been suggested by certain authors (Arayasirikul et al., 2020; Rotheram-Borus et al., 2018), which may offer an opportunity to offer ART adherence support and rapidly reach and scale prevention and treatment programs in this population.

These studies are not without limitations. First, when estimating the time from infection to diagnosis, we had a lot of missing data for CD4 count and did not use multiple imputation methods to address this issue. Multiple imputation is valid if its assumptions are valid. Given that we were unsure of the nature of the missingness of the data, we chose not to apply this approach. Therefore, our estimates of time from HIV to diagnosis may be overestimated or underestimated. Second, regarding our analytic cohort comprising of clients with two or more viral load tests, although we attempted to capture additional clients who had only one test in 2017 by including their last viral load test in 2016, our criteria restricted us from including clients who had only one suppressed viral load or no test throughout the period to ensure we had sufficient information to measure consistent viral suppression. This may have overestimated our findings. Finally, in computing person-time spent with viral load > 1500 copies/mL, we used each consecutive pair of viral load measurement. Even though we attempted to capture multiple viral loads to account for viral blips that may occur over time, it is not feasible to fully account for each client's complete viral load status throughout the observation period. In addition, our assessment of the psychosocial factors relied on information collected using non-standardized reporting instruments, which are subject to bias.

Taken together, the results of this dissertation show that we are still far from meeting the goals of the EHE initiative and Miami-Dade County's "Getting to Zero Initiative" to end HIV transmission in Florida. Policies increasing access to HIV testing and novel strategies promoting HIV screening in other alternative settings such as workplaces and ensuring HIV-self testing kits are readily available to the hard-to-reach population may be beneficial. Continued efforts to meet the specific HIV needs of underserved populations, particularly racial/ethnic minorities, must be supported by all

key players to fulfill the goals of the EHE initiative. In addition, adequate monitoring of programmatic outcomes, including reporting clients' maintained and sustained viral suppression status, may help optimize HIV care. Further research to determine which approaches are most effective in increasing HIV testing access in diverse settings with varying local needs can help shape additional ways to close the gaps in early diagnoses of HIV. Future research on undiagnosed and diagnosed PWH not retained in care is warranted to better understand their role in the HIV transmission dynamics.

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VITA

SEMIU OLATUNDE GBADAMOSI

Born: Lagos, Nigeria

2002-2008	M.B.B.S., Medicine & Surgery University of Lagos Lagos, Nigeria
2009-2010	Physician Intern Lagos University Teaching Hospital Lagos, Nigeria
2010-2012	Primary Care Physician Smith Medical Center Lagos, Nigeria
2013-2015	MPH Texas A&M University College Station, Texas
2015-2018	Research Fellow University of Nevada, Las Vegas Las Vegas, Nevada
2019-2020	Doctoral Student Florida International University Miami, Florida
2019-2021	Graduate Research Assistant Florida International University Miami, Florida
2020-Present	Doctoral Candidate Florida International University Miami, Florida
2021-Present	PhD Co-op, Global Data Science Merck & Co., Inc. Kenilworth, NJ

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