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## Developing Triage Tools for Retention in Care and Viral Suppression, and Identifying Predictors of Sexually Transmitted Infections among People with HIV

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FLORIDA INTERNATIONAL UNIVERSITY

Miami, Florida

DEVELOPING TRIAGE TOOLS FOR RETENTION IN CARE AND VIRAL  
SUPPRESSION, AND IDENTIFYING PREDICTORS OF SEXUALLY  
TRANSMITTED INFECTIONS AMONG PEOPLE WITH HIV

A dissertation submitted in partial fulfillment of

the requirements for the degree of

DOCTOR OF PHILOSOPHY

in

PUBLIC HEALTH

by

Merhawi Teklezgi Gebrezgi

2020

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

This dissertation, written by Merhawi Teklezgi Gebrezgi, and entitled Developing Triage Tools for Retention in Care and Viral Suppression, and Identifying Predictors of Sexually Transmitted Infections 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.

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Date of Defense: March 9, 2020

The dissertation of Merhawi Teklezgi Gebrezgi is approved.

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and Dean of the University Graduate School

Florida International University, 2020

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## DEDICATION

This dissertation is dedicated to my mother Lemlem Zerom and my father Teklezgi Gebrezgi who taught me to believe in my dreams, myself, and in God.

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ABSTRACT OF THE DISSERTATION  
DEVELOPING TRIAGE TOOLS FOR RETENTION IN CARE AND VIRAL  
SUPPRESSION, AND IDENTIFYING PREDICTORS OF SEXUALLY  
TRANSMITTED INFECTIONS AMONG PEOPLE WITH HIV

by

Merhawi Teklezgi Gebrezgi

Florida International University, 2020

Miami, Florida

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This study developed risk prediction tools for non-retention in HIV care and non-viral suppression, and identified factors associated with self-reported chlamydia and gonorrhea diagnosis among people with HIV (PHIV) in the Miami-Dade County Ryan White Program (RWP). Using retrospective cohort study data, we used stepwise logistic regression to develop score-based risk prediction tools for non-retention in care and non-viral suppression. We then used bootstrapping to internally validate the risk prediction tools. We also assessed the prevalence of self-reported chlamydia and gonorrhea diagnoses and factors associated with the diagnoses cross-sectionally using multivariate logistic regression.

Among the 7439 people meeting the inclusion criteria for the retention analysis, we found that non-retention in care in the next year could be predicted using current age, race, poverty level, homelessness, problematic alcohol/drug use and viral suppression status. The risk prediction tool had low discrimination (c-statistic=0.65), and the total score ranged from 0 to 17. Among the 6492 people meeting the inclusion criteria for the

viral suppression analysis, non-viral suppression in the next year could be predicted using current age, race, poverty level, AIDS status, homelessness, problematic alcohol/drug use and current viral suppression status. The risk prediction tool for non-viral suppression had good discrimination (c-statistic=0.77), and the total score ranged from 0 to 26.

Of the 7,419 adult PHIV in active Ryan White care during 2017, about half (n=3528) reported being screened for chlamydia or gonorrhea during 2017. Of these, 2.3% reported having been diagnosed with chlamydia or gonorrhea or both in 2017. Having a chlamydia or gonorrhea diagnosis was associated with being in the age group 18–39 and having multiple sexual partners during the previous 12 months.

In conclusion, using routinely available variables, we developed risk prediction tools for non-retention in care and non-viral suppression that can assist healthcare providers in identifying high-risk individuals to target for intervention. Both risk prediction tools need external validation. The risk prediction tool for non-retention in care additionally needs to include more prognostic factors in order to increase the discrimination. In order to prevent chlamydia or gonorrhea, targeted behavioral risk reduction techniques are highly recommended among those 18–39 years of age and those who have multiple sexual partners.



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## ABBREVIATIONS AND ACRONYMS

AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
FPL	Federal Poverty Level
HIV	Human immunodeficiency virus
IDU	Injection drug user
MAI	Minority AIDS Initiative
MSM	Men who have sex with men
OR	Odds ratio
PHIV	People with HIV
RWP	Ryan White Program
STI	Sexually transmitted infections
US	United States

## INTRODUCTION

Since the start of the human immunodeficiency virus (HIV) epidemic, about 75 million people have been infected with HIV (WHO, 2019; UNAIDS, 2019). Globally, by the end of 2018, there were approximately 39.9 million people living with HIV; and in the same year, 770,000 people died from HIV-related illnesses and 1.7 million people became newly infected with HIV (WHO, 2019; UNAIDS, 2019). In the United States, at the end of 2015, around 1.1 million people were living with HIV (Centers for Diseases Control and Prevention, 2018). Within the U.S., in 2017, Florida had the highest number of estimated new HIV infections followed by California and Texas (CDC, 2019(a)). In 2017, there were a total of 116,944 people with HIV (PHIV) in Florida (Florida Department of Health 2018 (a)).

Once diagnosed with HIV, PHIV need to be linked to care, take antiretroviral therapy (ART) and adhere to their medications to achieve successful HIV care outcomes. The HIV care continuum, also known as the HIV treatment cascade, includes a sequence of steps from initial diagnosis to achieving viral suppression. These steps are diagnosis of HIV infection, linkage to HIV care, retention in HIV care, adherence to ART, and viral suppression (U.S. Department of Health & Human Services, 2016). Retention in HIV care is a key step in ART adherence and viral suppression. Viral suppression (i.e. amount of HIV in the body is very low or undetectable) is the final and ultimate goal of the HIV care continuum and is usually a reflection of success in HIV care. It is important to monitor the proportion of PHIV engaged in each stage of the HIV care continuum, to help policymakers to identify the gaps and implement system

improvements and service enhancements that better support individuals as they move from one stage in the continuum to the next (U.S. Department of Health & Human Services, 2016).

Viral suppression (low viral load) benefits the individual living with HIV and the community. Virally suppressed individuals have slower disease progression, increased survival (Lima et al., 2007, Montaner 2011; Samji et al., 2013), and reduced risky sexual behavior (Mattson et al., 2014). At a community level, virally suppressed individuals are less likely to transmit the virus to others (Philbin et al., 2014; Cohen et al., 2011; Shah et al., 2016). Persons who are HIV infected but undiagnosed and persons who are HIV diagnosed but not retained in medical care were responsible for 91.5% of the estimated HIV transmissions in 2009 (Skarbinski et al., 2015). Therefore, by ensuring that everyone with HIV is aware of their infection and achieving viral suppression, HIV infections can be reduced.

In 2017, in the United States and six dependent areas, 86% of people living with HIV knew their status, 63% received medical care, 49% were retained in care and 51% were virally suppressed (Centers for Diseases Control and Prevention, 2017). The National HIV/AIDS Strategy 2020 aims to increase the number of HIV-positive individuals aware of their status to 90%, the proportion of persons with newly diagnosed HIV who are linked to care within one month to 85%, and the proportion of HIV-diagnosed individuals whose virus is effectively suppressed to 80% (CDC 2019(b)). Of all people living with HIV in Florida in 2017, 68% were retained in care (defined as having two or more documented viral load/CD4 laboratory results, medical visits or

prescription, at least three months apart in 2017) and 62% were virally suppressed (defined as a viral load <200copies/mL on the last viral load test in 2017) (Florida Department of Health 2018 (a)). In Miami-Dade County, of all people living with HIV in 2017, 64% were retained in care and 58% were virally suppressed (Florida Department of Health 2018 (b)).

Previous studies have found individual, social, behavioral and community factors associated with retention in care and viral suppression (Woodward et al., 2015; Bengtson et al., 2016; Giordano et al., 2009; Lourenço et al., 2014; Nosyk et al., 2015; Rebeiro et al., 2013; Tedaldi et al., 2014; Giordano, 2011; Robbins et al., 2010; Whiteside et al., 2014; Crepaz et al., 2018; Sheehan et al., 2017; Geter et al., 2018; Castel et al., 2016; Muthulingam et al., 2013; Tanner et al., 2016; Blank et al., 2015; Myers et al., 2016; Beer et al., 2016). These findings are amenable to being translated into validated and easy-to-use risk prediction tools to predict an individual's risk of not being retained in HIV care, or not achieving viral suppression (McNairy et al., 2017). Risk prediction tools are developed to identify patients at risk and to facilitate decision making. Factors to be included in the risk prediction tool should be routinely collected information, available to healthcare providers across diverse healthcare settings. Therefore, we used routinely collected sociodemographic, clinical, and laboratory information such as age, sex, race/ethnicity, alcohol/drug use, income level, living arrangement, transportation and food needs, acquired immunodeficiency syndrome (AIDS) status, initial viral loads, and other information to develop the risk prediction tool.

In addition to the type of exposure (such as blood transfusion), behavior (such as sharing needles or having sex without a condom), and high viral load (unsuppressed viral load), sexually transmitted infections (STIs) increase the risk of HIV transmission, (Centers for Diseases Control and Prevention, 2019 (c)). Sexually transmitted infections among PHIV increase HIV transmission through effects on HIV replication, HIV shedding, increases in viral diversity and through co-transmission of HIV with STIs (Galvin and Cohen 2004). Sexually transmitted infections among HIV-seronegative individuals also increase HIV susceptibility by mucosal disruption, immune changes in the genital tract, and effects on the genital tract microenvironment (Galvin and Cohen, 2004). The Centers for Diseases Control and Prevention (CDC) recommends annual STI screening among sexually active PHIV (Workowski & Bolan, 2015). Despite this recommendation, the rate of STIs screening among PHIV is suboptimal (Flagg et al., 2015; Quilter et al., 2017). Therefore, screening and monitoring for STIs among PHIV is an important standard of care in order to reduce HIV transmission.

The overall objectives of this dissertation were to develop a risk tool for retention in care, to develop a risk tool for viral suppression, and to identify predictors of sexually transmitted diseases among PHIV. In order to achieve this objective, we conducted three separate studies. The first study aimed to develop a risk prediction tool to identify people living with HIV who are at risk for non-retention in care. The second study aimed to develop a risk prediction tool to identify people living with HIV who are at risk of non-viral suppression. The third study aimed to identify predictors of chlamydia or gonorrhea diagnoses among PHIV. The first and second objectives address fundamental questions in the HIV care continuum by providing health care providers with risk prediction tools. By

using these tools, health care providers can predict individual's probability of falling out of HIV care or failing to achieve viral suppression in next year. If people likely to fall out of HIV care or to fail to achieve viral suppression are identified early, these people could be offered additional services to help them achieve retention and viral suppression. The third objective aimed to identify the main sociodemographic, behavioral and clinical predictors of chlamydia or gonorrhea diagnoses among PHIV. Understanding these factors can assist healthcare providers in their efforts to design interventions for PHIV who are at risk of developing these STIs. Ultimately, the results from this dissertation can improve client's retention, viral suppression, and STIs risk, and ultimately improve the quality of life of PHIV.

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## MANUSCRIPT 1

Gebrezgi M.T., Fennie K.P., Sheehan D.M., ... & Trepka MJ. (2020). Developing a triage tool for use in identifying people living with HIV who are at risk for non-retention in HIV care. *Int J STD AIDS*. In press.

### Abstract

**Introduction:** Identifying PHIV in HIV care who are at particular risk of non-retention in care is an important element in improving their HIV care outcomes. The purpose of this study was to develop a risk prediction tool to identify PHIV at risk of non-retention in care over the course of the next year.

**Methods:** We used stepwise logistic regression to assess sociodemographic, clinical and behavioral predictors of non-retention in HIV care. Retention in care was defined as having evidence of at least two encounters with an HIV care provider (or CD4 or viral load lab tests as a proxy measure for the encounter), at least 3 months apart within a year. We validated the risk prediction tool internally using the bootstrap method.

**Results:** The risk prediction tool included a total of six factors: age group, race, poverty level, homelessness, problematic alcohol/drug use, and viral suppression status. The total risk score ranged from 0 to 17. Compared to those in the lowest quartile (0 risk score), those who were in the middle two quartiles (score 1–4) and those in the upper quartile (>4 risk score) were more likely not to be retained in care (odds ratio [OR] 1.63 [CI; 1.39–1.92] and OR 4.82 [CI; 4.04–5.78] respectively). The discrimination ability for the prediction model was 0.651.

**Conclusions:** We found that increased risk for non-retention in care can be predicted with routinely available variables. Since the discrimination of the tool was low, future studies may need to include more prognostic factors in the risk prediction tool.

**Keywords:** non-retention, HIV, AIDS, risk prediction tool, risk score

## Introduction

The navigation of people with HIV (PHIV) across the HIV care continuum includes being diagnosed with HIV, linked to care, engaged in care, retained in care, adherent to antiretroviral therapy (ART), and having a suppressed HIV viral load (Kay et al., 2016). A goal of the United States (US) National HIV/AIDS Strategy is to increase the percentage of persons with diagnosed HIV who are retained in HIV medical care to at least 90 percent by 2020 (U.S. Department of Health & Human Services, 2015). The Centers for Diseases Prevention and Control (CDC) monitors retention in care using laboratory data from jurisdictions with complete reporting of CD4 and viral load test results. In 2015, only 57.2% of PHIV were retained in care (Centers for Disease Control and Prevention, 2019). Among 38 states with complete lab reporting for 2015 and 2016, none met the National HIV/AIDS Strategy 2020 target of 90%, 21 made progress toward the 2020 target, and 17 made no progress (Centers for Disease Control and Prevention, 2019).

Factors related to demographics, behavior, psychosocial and physical health affect retention in HIV care (Bulsara et al., 2016). Those factors include substance use (Giordano et al., 2009; Dombrowski et al., 2015; Centers for Diseases Control and

Prevention, 2018), belonging to a racial ethnic minority group (Giordano et al., 2009; Rebeiro et al., 2013; Giordano, 2011), mental health problems (Dombrowski et al., 2015; Centers for Diseases Control and Prevention, 2018), young age (Giordano et al., 2009; Nosyk et al., 2015; Lourenço et al., 2014; Tripathi et al., 2011), female gender (Giordano, 2011; Lourenço et al., 2014), injection drug use (IDU) as the vector for infection (Rebeiro et al., 2013; Giordano, 2011; Nosyk et al., 2015), having public health insurance (Tedaldi et al., 2014), health literacy (Waldrop-Valverde et al., 2013), intimate partner violence) Schafer et al., 2012), low socioeconomic status (Centers for Diseases Control and Prevention, 2018; Giordano, 2011), past-year missed treatment visits (Pence et al., 2018) and greater unmet socioeconomic needs such as housing, food, or transportation (Centers for Diseases Control and Prevention, 2018; Giordano, 2011). Some studies have synthesized these factors and devised a risk prediction tool to identify people who might be poorly retained in HIV care. A study attempted to develop a clinical decision tool to estimate the probability of being lost to follow-up among adults initiating antiretroviral therapy in resource-limited settings (McNairy et al., 2018). The study found that young age and advanced WHO disease stage were significant predictors of being lost to follow-up, but the model had weak ability to discriminate those who will remain in care from those who will be lost to follow-up. Another study developed a risk score to identify HIV-infected women who are most likely to be lost to follow-up in the postpartum period (Bengtson et al., 2016). Parity, education, employment status, WHO clinical stage, duration of combination ART during pregnancy, and number of antenatal care visits were found to predict being lost to follow-up. Woodward and his colleagues developed a risk prediction tool for medical appointment attendance among HIV-infected persons with

unsuppressed viremia (Woodward et al., 2015). They found that active substance abuse, poor adherence to daily medications, history of missing HIV care appointments, prior treatment failure, prior exposure to ART (defined as any prior exposure to nucleot(s)ide reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, and protease inhibitor classes OR a current regimen containing enfuvirtide), most recent CD4 lymphocyte count < 100 copies/mm<sup>3</sup>, and most recent viral load > 200 copies/mL predicted poor medical appointment attendance (Woodward et al., 2015).

Poor retention in care can lead to undesirable HIV outcomes at the individual and population levels (Giordano, 2011). Poor retention in care has been found to be associated with higher viral loads, lower CD4 cell counts (Tripathi et al., 2011), higher rates of ART failure, decreased likelihood of receiving antiretroviral therapy, increased HIV transmission risk behavior, increased hospitalization rates, and worse survival (Giordano, 2011). Therefore, retention in HIV care is a key step to improve HIV outcomes and overall health of PHIV. The aim of this study was to identify people in HIV care who are likely to be poorly retained in care over the course of the following year using sociodemographic, clinical, and laboratory information.

## Methods

We used retrospective data from the Miami-Dade County (Florida) Ryan White Program (RWP) Part A/ Minority AIDS Initiative (MAI) for the calendar years 2016–2017 to assess the relationship between sociodemographic, clinical and behavioral variables and risk of non-retention in HIV care, with a primary focus on routinely available variables. The RWP Part A provides core medical, medical case management,

pharmaceutical, and related support services to low-income people with HIV in metropolitan areas heavily impacted by HIV/AIDS (“Eligible Metropolitan Areas,” or EMAs), to improve their access to HIV care and their health outcomes; the MAI program provides additional support for a subset of these services, targeted toward ethnic and racial minorities in these EMAs.

#### Study population

The population was PHIV who were enrolled in (and receiving services from) the RWP Part A/MAI program in the Miami-Dade EMA in 2016. Enrollment was defined as having received at least one medical case management encounter or peer education support network service in 2016. We measured risk factors in 2016, and the outcome (non-retention in care) was measured in 2017. Risk factors were obtained from the RWP’s comprehensive health assessment, patient intake assessment and laboratory results entered into the patient’s electronic medical records. The comprehensive health assessment is a health and social needs assessment of RWP patients that is completed every 6 months to determine the plan of care and needs for referrals to other services. Patient intake assessment includes demographic data collected at time of entry into the RWP. We excluded people who had no comprehensive health assessment in 2016, or were <18 years old in January 2016, who died in 2016 or 2017, or were out-of-network referrals in 2016 or 2017. Out-of-network referrals are people who were referred to the RWP from a non-RWP provider, receiving a single service but not receiving regular medical case management, and for whom data about retention would not be available. We also excluded clients if their case was closed because of movement to another



state/county, financial ineligibility, or incarceration greater than 6 months in 2016 and 2017. Moreover, clients diagnosed with HIV in 2016, and those who received their first RWP care in 2016 but who had no viral load measurement in 2016 were excluded from the analysis. We deleted four people who had missing information about problematic alcohol/drug use in 2016.

## Measurements

The following variables were considered in the development of the risk prediction model: age (18–24, 25–39 and  $\geq 40$  years), sex assigned at birth (male/female), race (Black/other), transgender status (yes/no), Hispanic ethnicity (yes/no), homelessness (includes homeless patients and patients in transient or transitional housing) (yes/no), CDC-defined AIDS status as of 2016 (yes/no), viral suppression in 2016 (yes/no), getting the food he/she needs (yes/no), access to transportation for healthcare/dental/social service appointments (yes/no), alcohol/drug use resulting in any legal problems, hazardous situations or problems in patient's daily activities, history of injection drug use, including injection drug use as the self-reported vector for the original HIV infection (yes/no), self-reported feelings of depression or anxiety (yes/no), and income <100% of the federal poverty level (FPL) (yes/no). Federal poverty level <100% in 2016 was defined as having a household income less than \$11,880 for a single person (United States Department of Health and Human Services, 2016). Problematic alcohol/drug use was derived from three questions namely: (a) Has alcohol/drug use resulted in hazardous situation, (b) Has alcohol/drug use resulted in legal problems, and (c) Is your alcohol/drug use preventing you from carrying out your daily activities?

History of injection drug use (IDU) includes injection drug users, and men who have sex with men who are also injection drug users.

## Outcome

The outcome of the study was non-retention in HIV care in 2017. We defined retention in care as having evidence of at least two occurrences of any combination of (a) face-to-face encounter(s) with a Ryan White Program medical care professional, or (b) laboratory tests (CD4 or viral load), at least three months apart during 2017.

## Analysis

First, we selected risk factors to be included in the bivariate analysis based on evidence from literature and completeness of information in the dataset, and we estimated unadjusted odds ratios. Variables associated with non-retention in HIV care at  $p$ -value  $< 0.1$  in bivariate analysis were included in the initial multivariate logistic regression model. We used stepwise backward elimination, retaining variables which maintained significance at  $P < 0.05$  in the final model. We used Akaike information criterion (AIC) to check the model fit (Lee et al., 2016). We checked for any confounding effect of the excluded variables in the final model. Discrimination was assessed using concordance statistic or C-statistic (which is equal to the area under the receiver operating characteristic [ROC] curve), and calibration was assessed using calibration plots by dividing subjects into deciles of risk (Steyerberg et al., 2010).

We validated the risk score tool internally using the bootstrap method with the original derivation data set. A total of 1000 samples were created by sampling with

replacement, and each bootstrap sample was the same size as the original derivation sample. For each sample, the model was refitted following the same method adopted in the derivation process. We computed model performance (C-statistic) on each bootstrap sample and compared it with the model performance in the original data to calculate optimism (magnitude of bias). The optimism-adjusted C-statistic was computed by subtracting the optimism from the original C-statistic (Steyerberg, 2009).

Finally, we generated a simple integer-based risk score for each predictor variable by multiplying the beta coefficients by 10 and rounding to the nearest integer (Bengtson et al., 2016; Steyerberg, 2009). The total risk score was calculated by adding each component together. We divided the population into strata based on quartiles of the total risk score by placing cut points at the 25<sup>th</sup>, 50<sup>th</sup> and 75<sup>th</sup> percentiles (Traeger et al., 2015; Chan et al., 2012). We also calculated the sensitivity and specificity at each risk score cutoff point. The predictive performance of the risk score was evaluated by means of discrimination and calibration. All analyses were conducted using SAS software V. 9.4 (SAS Institute Cary, NC). This study was approved by the Florida International University Institutional Review Board.

## Results

Of the total 9011 PHIV enrolled in RWP in 2016, 7439 people were included in our analysis. A total of 1572 PHIV were excluded for various reasons (Figure 1). About 24% (1759) of the 7439 were not retained in HIV care during 2017. The mean age and standard deviation of the study population was  $44.4 \pm 11.9$  years. About 64% of the

population were older than 40 years, 59.7% were Black, 76.2% were male, and 55.7% were Hispanic (Table 1).

Of the 14 potential variables considered, 11 variables were associated with non-retention in HIV care at  $p$ -value  $<0.1$ . In the bivariate analysis, age in 2016, race, poverty level, homelessness, alcohol/drug use resulting in any problem in daily activity, legal issue or hazardous situation, viral suppression status, Hispanic ethnicity, feeling depressed or anxious and food need were significant at  $p$ -value  $<0.001$ ; whereas history of IDU and access to transportation were significant at  $p$ -value  $<0.05$  (Table 1). Sex assigned at birth, transgender status, and AIDS status as of 2016 were not associated with retention in care in 2017 ( $p$ -value  $>0.1$ ). In the stepwise logistic regression analysis, six variables maintained significance level at  $p$ -value  $<0.05$  level in the final model (Table 1). The six variables were age, race, poverty level, homelessness, alcohol/drug use resulting in any problem in daily activity, legal issue or hazardous situation, and viral suppression status. The discrimination of the overall model with the 6 variables was 0.654 (Figure 2(a)), and after adjusting for optimism, the discrimination was 0.651. Based on the calibration plot, the agreement between the observed and predicted proportion of events of non-retention in HIV care showed good apparent calibration (Figure 2(b)).

The final risk prediction tool included 6 risk factors present in 2016 that can be used to predict non-retention in HIV care over the course of 2017 (Figure 3). Each risk factor contributed additively to an overall risk score, as follows: having unsuppressed viral load had a risk score of 5, being homeless had a risk score of 3, being Black had a

risk score of 2, being in the age group 18-24 had a risk score of 1, being in the age group 25-39 had a risk score of 2, having income below 100% of the federal poverty level had a risk score of 1, and alcohol/drug use resulting in any problem in daily activity, legal issue or hazardous situation had a risk score of 4. The minimum total risk score was 0 for a person without any of the risk factors, and the maximum possible risk score was 17. A person with a total risk score of 0 had 14.4% probability of not being retained in HIV care in 2017, and a person with a total risk score of 17 had 82.5% probability of not being retained in HIV care. As the risk score increased, the probability of non-retention in care increased. Every one-point increase in the risk score scale was associated with OR 1.22 (95% CI; 1.20–1.24) increase in non-retention in care. The discrimination of the risk score was 0.650. We divided the risk scores into three categories based on quartiles placing cut points at the 25th and 75th percentiles. There were 1559 (21.0%) people in the first quartile (0 risk score), and 211 (13.5%) of these were not retained in HIV care. In the second and third quartiles (score 1–4), there were 4331 (58.2%) people, and in the upper quartile (>4 risk score) there were 1549 people (20.8%). About 20% (882) of those in the second and third quartiles and 43.0% (666) of those in the upper quartile were not retained in HIV care. Compared to those in the first quartile, those who were in the middle two quartiles and those in the upper quartile were more likely not to be retained in care (OR 1.63 [CI; 1.39–1.92] and OR 4.82 [CI; 4.04–5.78], respectively). The cutoff value of 4 had a sensitivity of 43% and specificity of 80% and a cutoff value of 5 had a sensitivity of 38% and specificity of 84%. Similarly, a cutoff value of 3 in the risk score had a sensitivity of 56% and specificity of 65%.

## Discussion and Conclusion

In this study, we derived and internally validated a risk prediction tool for non-retention in HIV care in the next year using retrospective data from Miami-Dade County RWP Part A/MAI. This risk prediction tool can be used in clinical settings by HIV care providers to identify PHIV who will not be retained in HIV care in the next year. We found that the risk score constitutes age group, race, poverty level, homelessness, problematic alcohol/drug use and viral suppression status. These variables can be extracted easily from medical records or by interviewing the patient and can be implemented in a variety of settings.

The individual factors included in our risk prediction tool have been previously found to predict retention in care. Consistent with findings in previous studies, unsuppressed viral load and age group predict retention in HIV care (Giordano et al., 2009; Nosyk et al., 2015; Lourenço et al., 2014; Tripathi et al., 2011; McNairy et al., 2018; Woodward et al., 2015). Similarly, persons living with HIV who are homeless or have low economic status have been found to be poorly retained in care ) (Centers for Diseases Control and Prevention, 2018; Giordano, 2011; Rajabiun et al., 2018; Wolitski et al., 2007). This is likely due to unmet social service needs (Wolitski et al., 2007). People who use alcohol/drugs are at increased risk of poor adherence and non-retention in HIV care (Vagenas et al., 2015; Edison et al., 2014; Williams et al., 2016; Gwadz et al., 2016). This may be due to the behavioral factors associated with alcohol/drug use. Moreover, being Black/African American has been identified as a risk factor increasing non-retention in care. Historical and cultural factors as well as structural racism may

affect the retention of African Americans in HIV care (Freeman et al., 2017). Therefore, inclusion of Black race in the risk prediction tool is likely a proxy for underlying social, cultural, and economic factors. Inclusion of race in the risk prediction tool may lead to unconscious bias by health care providers about Blacks. Addressing racial bias needs comprehensive, multifaceted, and evidence-based interventions at the individual and organizational level including leadership commitment to a cultural inclusion, diversity training, self-reflection on personal biases, mentorship and sponsorship, and cultural competency (Marcelin et al., 2019).

We stratified the population into quartiles, and patients with a total risk score  $>4$  were classified in the fourth quartile. The risk of non-retention in care showed a graded increase across the quartiles. Those who were in the fourth quartile were about 5 times more likely not to be retained in care than those who were in the first quartile. A cutoff value of 5 in the risk score had a sensitivity of 38% and a specificity of 84%. This cutoff identified 20.8% of our study population with the highest likelihood of non-retention in care for intervention. Based on this risk score cutoff, non-viral suppression, independent of other factors in the risk score, contributes to one third of the total risk score. Thus, viral suppression is a good predictor to use for identifying patients that may benefit from a retention intervention. Alternatively, a lower cutoff point in the risk score would yield higher sensitivity and lead to targeting a larger proportion of the population for a retention intervention.

Previous risk prediction tools developed to predict patient adherence to appointments or retention in care were either restricted to specific populations or had

different outcome definitions. The study by McNairy et al. measured lost to follow-up based on a single clinic or pharmacy visit during 365 days after ART initiation (McNairy et al., 2018). Our definition of retention in care was based on two or more clinic visits or laboratory tests at least three months apart during a year. Bengtson et al. developed a risk prediction tool among HIV-infected women, and they included different predictors specific to pregnant women such as parity and number of antenatal care visits (Bengtson et al., 2016). Woodward et al. used a tool previously developed for virologic failure to stratify patients based on medical appointment attendance (defined based on a single visit) among persons with unsuppressed viremia (Woodward et al., 2015). The definition of the outcome and the target population are different from ours. Some factors such as substance use and viral suppression were common predictors in our risk prediction tool and theirs. However, Woodward et al included additional predictors such as prior treatment failure, adherence to daily medications, history of missing HIV care appointments, and prior exposure to ART which may be better predictors of retention in care but are not readily collected in our study.

The risk prediction tool is intended to be used in HIV care settings, where the characteristics of the target population are similar to ours. Upon arrival of a patient to the HIV care setting, an HIV care provider could assess the probability of a patient not being retained in HIV care in the next year using this checklist. Depending on the availability of resources, HIV care providers may arrange for an intervention to support retention based on severity of risk in order to improve HIV outcomes (Samji et al., 2013; Montaner, 2011) and reduce HIV transmission (Cohen et al., 2011; Shah et al., 2015). Retention in HIV care can be improved by incorporating informational, motivational, and behavioral



skill components (Giordano, 2011). Peer navigators and clinic-wide marketing (e.g., posters, brochures) including targeted messages on staying in care which were delivered at minimal effort and cost, have been found to be effective in improving clinic attendance (Centers for Diseases Control and Prevention, 2018; Gardner et al., 2012; Gardner et al., 2015). Designating a staff person to help with appointments, referrals, system navigation, service coordination, and transportation may improve retention in HIV care (Centers for Diseases Control and Prevention, 2018; Okeke et al., 2014). Enhancing personal contact with patients and asking open-ended questions in regular conversations at every office visit may help to identify specific ART adherence and retention support services (Centers for Diseases Control and Prevention, 2018; Gardner et al., 2014).

Our study has several limitations. First, in our analysis, we included variables that are routinely collected and easily available to care providers. However, these variables were not strong predictors of non-retention in care. The discriminative ability of our study is low (0.651) (Lloyd-Jones et al., 2010), although it is higher than that of the study by McNairy et al (McNairy et al., 2018). Moreover, we were not able to find a risk score cutoff with higher sensitivity and specificity. This indicates that other predictive variables could have been included in the risk prediction tool to improve its discriminative ability. Factors such as adherence to daily medications, sexually transmitted infections, previous appointment attendance, prior treatment failure (Woodward et al., 2015), and other unmet needs (Centers for Diseases Control and Prevention, 2018; Giordano, 2011) may increase the discriminative ability of the risk prediction tool. However, information about these factors may not be routinely accessible to the HIV care providers, or collecting these factors may require additional resources and increase the workload for HIV care

providers or support staff. Although the discrimination level is relatively low, this tool can be used in situations where these additional variables are not available. Second, we used RWP Part A/MAI data to develop and internally validate our risk prediction tool. The Ryan White Program provides medical care, medical case management, anti-retroviral prescription drugs and other support for PHIV without health insurance. Thus, Ryan White Program participants may not be representative of all PHIV. Third, people newly diagnosed with HIV may behave differently due to experiencing additional challenges related to acceptance of their diagnosis and stigma. Therefore, they may require a different risk prediction tool. Finally, of those enrolled in 2016, we were not able to find laboratory results for 917 people during 2017. In a separate analysis, we excluded those people, and the results were similar with the model that included those 917 people.

In summary, we developed a relatively simple prediction tool that can be used to identify PHIV who are at risk of non-retention in HIV care. This tool includes characteristics that are routinely collected in healthcare settings. These factors include age group, race, poverty level, homelessness, problematic alcohol/drug use and viral suppression status. The risk prediction tool has low discrimination power but could be a good alternative tool in situations where additional data is not available. Further research should include better predictive variables to enhance the accuracy of this risk prediction tool.

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Tables and figures

Table 1. Population characteristics and model of risk variables associated with non-retention in care among PHIV (N=7439)

Characteristics during 2016	Total population (n)	Not retained in care n (%)	Bivariate analysis		Multivariate analysis		
			Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	Coefficient (Beta)	Score
Total	7439	1759 (23.7)					
Age (years)				<0.001			
18–24	413	142 (34.4)	1.85 (1.57–2.42)		1.51 (1.21–1.90)	0.05	1
25–39	2256	608 (30.0)	1.38 (1.22–1.54)		1.31 (1.16–1.48)	0.21	2
≥40	4770	1009 (21.2)	Ref		Ref		
Race				<0.001			
Other	4443	889 (20.0)	Ref		Ref		
Black	2996	870 (29.0)	1.64 (1.47–1.82)		1.37 (1.22–1.53)	0.16	2
Income below 100% of FPL				<0.001			
No	4178	840 (20.1)	Ref		Ref		
Yes	3261	919 (28.2)	1.56 (1.40–1.74)		1.24 (1.11–1.40)	0.11	1
Homeless				<0.001			
No	6983	1567 (22.4)	Ref		Ref		
Yes	456	192 (42.1)	2.51 (2.07–3.05)		1.80 (1.46–2.23)	0.27	3
Alcohol/drug use resulted in any problem in daily activity, legal issue or hazardous situation				<0.001			
Yes	192	106 (55.2)	4.17 (3.12–5.57)		2.36 (1.72–3.23)	0.43	4
No	7247	1653 (22.8)	Ref		Ref		
Virally suppressed				<0.001			
Yes	6232	1224 (19.6)	Ref		Ref		
No	1207	535 (44.3)	3.26 (2.86–3.71)		2.69 (2.35–3.07)	0.49	5
Sex assigned at birth				0.56			

Male	5667	1349 (23.8)	Ref	
Female	1772	410 (23.1)	1.04 (0.92–1.18)	
Hispanic ethnicity				<0.001
Yes	4143	813 (19.6)	Ref	
No	3296	846 (25.7)	1.41 (1.28–1.58)	
Are you feeling depressed or anxious?				<0.001
Yes	1146	305 (30.5)	1.52 (1.33–1.75)	
No	6293	1409 (22.4)	Ref	
Are you getting the food you need?				<0.001
Yes	7322	1717 (23.5)	Ref	
No	117	42 (35.9)	1.83 (1.25–2.68)	
CDC-defined AIDS				0.13
Yes	3041	746 (24.5)	1.09 (0.98–1.21)	
No	4398	1013 (23.0)	Ref	
History of IDU				0.030
No	7309	1714 (23.5)	Ref	
Yes	130	45 (34.6)	1.73 (1.20–2.49)	
Access to transportation to appointments				0.01
Yes	6726	1563 (23.2)	Ref	
No	713	196 (27.5)	1.25 (1.05–1.49)	
Transgender				0.44
No	7396	1751 (23.7)	Ref	
Yes	43	8 (18.6)	0.74 (0.34–1.59)	

OR: Odds Ratio; FPL: Federal Poverty Level; IDU: Injection Drug Use; AIDS: Acquired Immunodeficiency Syndrome; CI: Confidence Interval; CDC: Centers for Diseases Control and Prevention

The multivariate logistic model included variables that were significant at p-value <0.1 in the bivariate analysis. These include all the variables in the table except sex assigned at birth, AIDS status and transgender status.

Scores were assigned to each risk factor by multiplying each beta obtained from the stepwise logistic regression model by 10.



Figure 1. Diagram for exclusion of participants from the present study

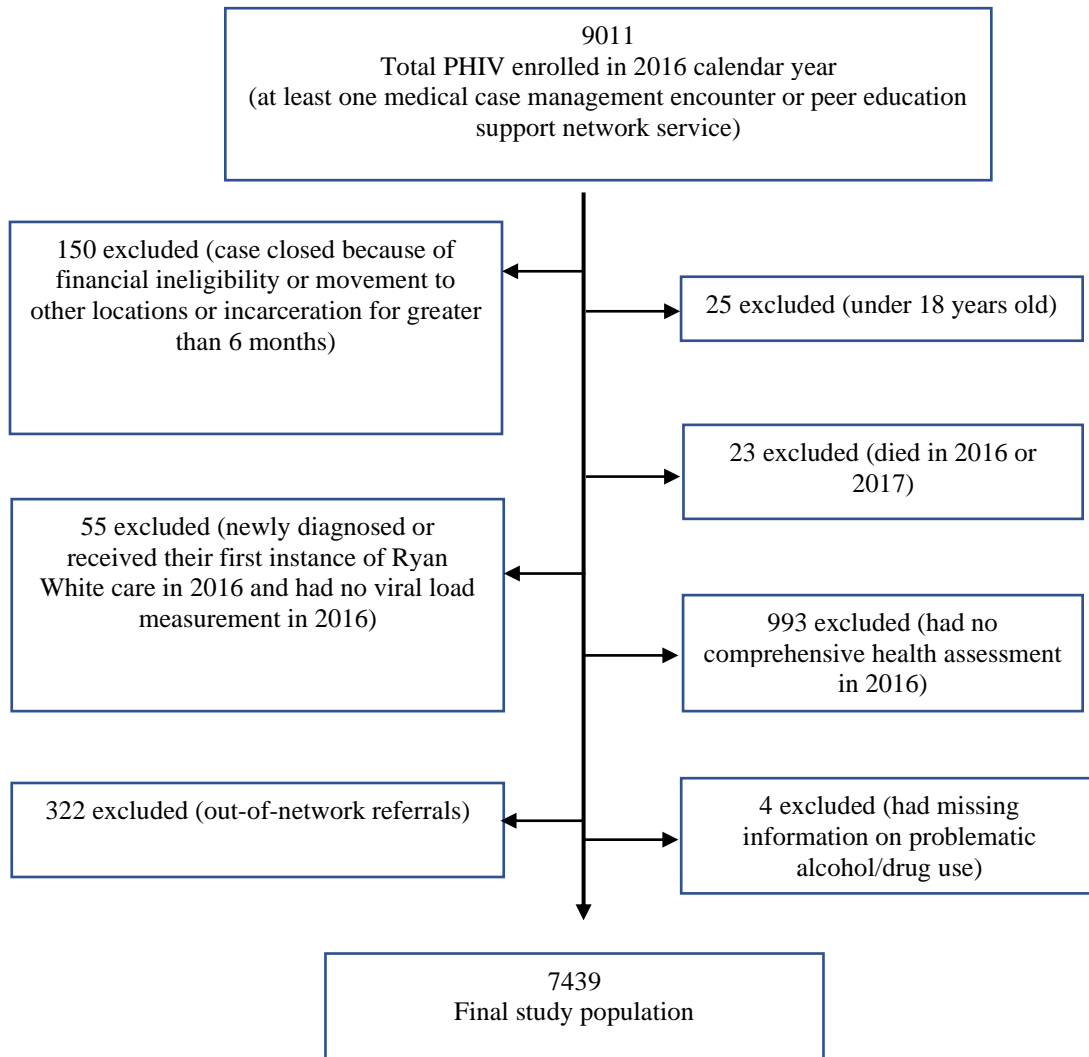


Figure 2. a) Discrimination of the final model b) Calibration of the final model

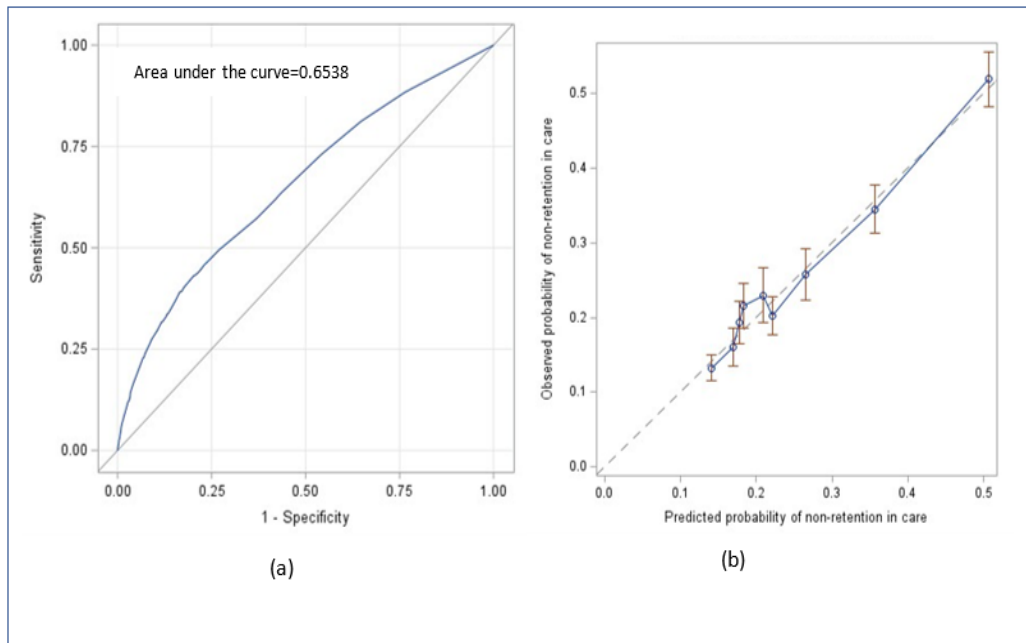


Figure 3. Point scores for all risk factors in the logistic regression model

Characteristics at baseline	Categories	Scores values		Score	Probability of non-retention in following year (%)
Age (years)	18–24	1 <input type="checkbox"/>		0	14.4
	25–39	2 <input type="checkbox"/>		1	17.0
	≥40	0 <input type="checkbox"/>	Score: <input type="checkbox"/>	2	19.9
Race	Other	0 <input type="checkbox"/>		3	23.2
	Black	2 <input type="checkbox"/>	Score: <input type="checkbox"/>	4	26.9
Income less than 100% of federal poverty level	No	0 <input type="checkbox"/>		5	31.0
	Yes	1 <input type="checkbox"/>	Score: <input type="checkbox"/>	6	35.3
Homeless	No	0 <input type="checkbox"/>		7	39.9
	Yes	3 <input type="checkbox"/>	Score: <input type="checkbox"/>	8	44.7
Alcohol/drug use resulted in any problem in daily activity or legal issue or hazardous situation	Yes	4 <input type="checkbox"/>		9	49.7
	No	0 <input type="checkbox"/>	Score: <input type="checkbox"/>	10	54.5
Virally suppressed	Yes	0 <input type="checkbox"/>		11	59.3
	No	5 <input type="checkbox"/>	Score: <input type="checkbox"/>	12	63.9
Total Score: <input type="checkbox"/>				13	68.3
				14	72.4
				15	76.1
				16	79.5
				17	82.5

The predicted probabilities of non-retention in HIV care for the total risk score ranged from 14.2% for a patient with 0 total score to 82.5% for a patient with 17 total score. To get the total score for individual person, we should add the scores of the six variables. For example, for patient who is 20 years old (Score=1), White (Score=0), income equal to or higher than 100% of FPL (Score=0), homeless (Score=3), with no problematic alcohol/drugs use (Score=0), and has unsuppressed viral load (Score=5), the total score will be 9 (1+0+0+3+0+5). A person with total score of 9 had 49.7% probability of not being retained in care in the next year.

## MANUSCRIPT 2

Gebrezgi M.T., Fennie K.P., Sheehan D.M., ... & Trepka MJ. (2020). Development and validation of a risk prediction tool to identify people living with HIV likely not to achieve viral suppression. *AIDS Pt Care and STDs*. In press.

### **Abstract**

**Introduction:** Identifying people with HIV (PHIV) who are at risk of not achieving viral suppression is important for targeted intervention. The aim of this study was to develop and test a risk prediction tool for PHIV who are at risk of not achieving viral suppression after a year of being in care.

**Methods:** We used retrospective data to develop an integer-based scoring method using backward stepwise logistic regression. We also developed risk score categories based on the quartiles of the total risk score. The risk prediction tool was internally validated by bootstrapping.

**Results:** We found that non-viral suppression after a year of being in care among PHIV can be predicted using seven variables, namely; age group, race, federal poverty level, current AIDS status, current homelessness status, problematic alcohol/drug use and current viral suppression status. Those in the high-risk category had about 23 increase in the odds of non-viral suppression compared to the low-risk group. The risk prediction tool has good discriminative performance and calibration.

**Conclusions:** Our findings suggest that non-viral suppression after a year of being in care can be predicted using routinely available variables. In settings with similar demographics, the risk prediction tool can assist healthcare providers in identifying high-risk individuals to target for intervention. Follow-up studies are required to externally validate this risk prediction tool.

**Keywords:** HIV, AIDS, viral suppression, risk prediction tool, risk score

## Introduction

In the United States, at the end of 2015, about 1.1 million people were living with HIV, and in 2015, there were an estimated 38,000 new HIV infections (Centers for Diseases Control and Prevention, 2018). In 2017, Florida had the highest number of estimated new HIV infections (4800) (Centers for Diseases Control and Prevention, 2018(a)). Within Florida, Miami-Dade County had the highest number of people with HIV (PHIV); approximately 29,969 in 2017 (Florida Department of Health, 2018).

Once diagnosed with HIV, PHIV need to be linked to and retained in care, take antiretroviral therapy (ART) and adhere to their medications in order to have successful HIV care outcomes. The HIV care continuum, defined as stages of HIV medical care that PHIV go through, from initial diagnosis to achieving viral suppression (U.S. Department of Health & Human Services, 2016), includes five steps, namely HIV diagnosis, linkage to HIV care, retention in HIV care, adherence to ART, and viral suppression (Kay et al., 2016). Viral suppression is the final step and ultimate goal of the HIV care continuum and is usually a reflection of success in HIV care. Viral suppression benefits the

individual living with HIV and the community. Virally suppressed PHIV have slower disease progression and increased survival (Lima et al., 2007; Montaner, 2011; Samji et al., 2013). At the community level, virally suppressed individuals are less likely to transmit the virus to others (Philbin et al., 2014; Cohen et al., 2011; Shah et al., 2015). Despite the availability of ART, a substantial number of PHIV are not virally suppressed (Centers for Diseases Control and Prevention, 2017). For example, in 2015, in 39 US states and District of Colombia, 40.2% of the PHIV were not virally suppressed (Centers for Diseases Control and Prevention, 2018(b)).

Given the importance of viral suppression, there is a need to develop evidence-based strategies to monitor and predict this outcome. There are numerous cross-sectional and longitudinal studies which have identified factors associated with viral suppression among PHIV (Crepaz et al., 2018; Whiteside et al., 2014; Sheehan et al., 2017; Joseph Davey et al., 2018; Geter et al., 2018; Castel et al., 2016; Colasanti et al., 2015; Muthulingam et al., 2013; Tanner et al., 2016; Blank et al., 2015; Myers et al., 2016; Beer et al., 2016). These factors include young age (Crepaz et al., 2018; Whiteside et al., 2014), gender (Whiteside et al., 2014; Sheehan et al., 2017; Joseph Davey et al., 2018), Black race (Crepaz et al., 2018; Sheehan et al., 2017; Geter et al., 2018; Castel et al., 2016; Colasanti et al., 2015), unstable housing (Muthulingam et al., 2013), substance use, higher baseline viral load (Tanner et al., 2016), long duration of HIV infection (Castel et al., 2016), poor general health status (Castel et al., 2016; Blank et al., 2015), being US born (Myers et al., 2016), and low educational attainment (Beer et al., 2016). There is a need to translate these findings about individual factors into validated and easy-to-use risk tools for use in predicting an individual's risk of not achieving viral suppression.

Studies have been conducted to develop risk prediction tools for virologic failure (Robbins et al., 2010), and for predicting extended high viremia among newly diagnosed people (Powers et al., 2018). Clinical and behavioral factors related to sub-optimal adherence, recent CD4 count, drug and/or alcohol abuse, prior ART exposure, prior treatment failure, and recent HIV-1 viral load were used to predict virologic failure after one year among those who were virologically suppressed on ART at enrollment (Robbins et al., 2010). Researchers have also developed risk prediction tools for HIV disease progression, particularly for mortality (Mocroft et al., 2007; Bebu et al., 2014; Nugent et al., 2014). The aim of our study was to develop and test a risk prediction tool for PHIV who are in care but are at risk of not achieving viral suppression after a year of being in care, to use for triaging those in need of more assistance. If people likely not to achieve viral suppression are identified early, intervention strategies could be implemented to assist these individuals into achieving viral suppression and ultimately improve their quality of life (National Institute of Health, 2015).

## Methods

### Data source and study population

We developed and internally validated a risk prediction tool for non-viral suppression using retrospective data from the Miami-Dade County Ryan White Program (RWP) Part A/ Minority AIDS Initiative (MAI) for the calendar years 2016–2017. The dataset included 6492 PLWH who were in care in 2016 and 2017 in the RWP Part A/MAI. In care was defined as having at least one viral load or cluster of differentiation 4

(CD4) count test in each year. All exposures were measured in 2016, and viral suppression was measured in 2017.

The Ryan White Program is a comprehensive system of care for PHIV. It provides primary medical care and other support for PHIV without health insurance. In the US, more than half of PHIV receive services through the Ryan White HIV/AIDS Program each year (Ryan White HIV/AIDS Program, 2019). The Ryan White Program services include outpatient/ambulatory health services, oral health care, other professional services (legal services and permanency planning), food bank, medical transportation (in the form of vouchers), mental health services, medical case management (including treatment adherence), health insurance premium and cost sharing assistance, local AIDS pharmaceutical assistance, substance abuse care and services (both outpatient and residential), and outreach services.

#### Predictor variables

We selected sociodemographic, clinical and behavioral variables based on evidence from the literature and completeness of information in the dataset (Crepaz et al., 2018; Whiteside et al., 2014; Sheehan et al., 2017; Joseph Davey et al., 2018; Geter et al., 2018; Castel et al., 2016; Colasanti et al., 2015; Muthulingam et al., 2013; Tanner et al., 2016; Blank et al., 2015; Myers et al., 2016; Beer et al., 2016). All characteristics were parameterized as categorical variables and refer to the year 2016. Age was categorized as 18–24, 25–39, and  $\geq 40$  years. All other variables were binary and included sex assigned at birth (male/female), homelessness (yes/no), race (Black/ White or other), transgender (yes/no), Hispanic ethnicity (yes/no), alcohol/drug use resulting in any problem in



patients daily activity or legal issue or hazardous situation (referred as problematic alcohol/drug use in this manuscript) (yes/no), self-reported feelings of depression or anxiety (yes/no), patient getting the food he/she needs (yes/no), patient had CDC-defined AIDS as of 2016 (yes/no), patient virally suppressed in 2016 based on the last viral load laboratory test in 2016 (yes/no), patient had access to transportation for healthcare/dental/social service appointments (yes/no), patient had a history of injection drug use (yes/no), and federal poverty level (FPL) <100% (yes/no). Federal poverty level <100% in 2016 was defined as having a household income less than \$11,880 for a single person (United States Department of Health and Human Services, 2016). We defined problematic alcohol/drug use as having any of the following; (a) Has alcohol/drug use resulted in legal problems? (b) Has alcohol/ drug use resulted in hazardous situation? and (c) Is your alcohol/drug use preventing you from carrying out your daily activities? All predictor variables were obtained from the patient intake assessment (information collected at time of entry into the RWP Part A/MAI, comprehensive health assessment (bi-annual assessment of all RWP Part A/MAI patients) or laboratory data.

## Outcome

The outcome, viral suppression, was a binary variable, and non-viral suppression was defined as having viral load  $\geq 200$  copies/mL in the last viral load measurement in 2017 (Centers for Diseases Control and Prevention, (2018(c))).

## Inclusion and exclusion criteria

We included PHIV who were in care in 2016 and 2017 and who had a comprehensive health assessment in 2016. Comprehensive health assessment is a health and social needs assessment of a Ryan White Program patients that is completed every 6 months to determine plan of care and need for referrals to other services. Patients who were less than 18 years old in January 2016, died in 2016 or 2017, had no comprehensive health assessment in 2016, or were out-of-network referrals in 2016 or 2017 were excluded. Out-of-network referrals are people who were referred to the RWP from a non-RWP provider. Patients whose case was closed because of moving to another state/county, financial ineligibility, or incarceration for greater than six months during 2016 or 2017 were also excluded.

## Analysis

First, we conducted bivariate analysis to assess the association between each predictor variable and the outcome and estimated crude odds ratio (OR). All variables associated with non-viral suppression at  $p < 0.1$  in the bivariate analysis were included in the initial logistic regression model. With stepwise backward elimination, we retained only significant factors ( $P < 0.05$ ) in the final model (Steyerberg, 2009).

We assessed calibration using calibration plots by dividing subjects into deciles of risk according to their model predictions, and the observed non-viral suppression levels among the subjects. Each decile was plotted against the average predicted probability of non-viral suppression and compared to the 45° line (perfect calibration) (Steyerberg et al.,

2010). The ability of the prediction model to distinguish events versus non-events (discrimination) was measured by the concordance statistic or C-statistic (which is equal to the area under the receiver operating characteristic (ROC) curve) (Steyerberg et al., 2010).

We assessed internal validity with a bootstrapping procedure, extracting 1,000 samples with replacement, of the same size as the original data set ( $n = 6,492$ ) (Steyerberg et al., 2001; Han et al., 2016). For each sample, we used the same procedure that was used in the original dataset (stepwise backward logistic regression model). Then we calculated optimism by comparing the final model performance (C-statistic) of bootstrap samples with that of the original data. The bootstrap-corrected C-statistic was computed by subtracting the optimism from the original C-statistic (Steyerberg, 2009).

#### Risk score development

We aimed to develop a simple risk score tool that could be easily assessed in a variety of settings to identify PHIV who are at risk of not achieving viral suppression after a year of being in care. After obtaining the beta coefficients from the final logistic regression model, the scores for each predictor were determined by multiplying each beta coefficient by 10 and rounding to the nearest integer (Steyerberg, 2009; Austin et al., 2016).

The total risk score was calculated by adding the scores for all existing risk factors. In order to develop an easily interpretable method to classify patients according to the risk of not achieving viral suppression, we divided the risk score into three strata

(by placing cut points at the 25th and 75th percentiles of the model's total risk score distribution). We also calculated sensitivity, specificity, positive predictive value, and negative predictive value for a range of potential cutoff points. All statistical analyses were performed using SAS software version 9.4 (SAS Institute Cary, NC). This study was approved by the Florida International University Institutional Review Board.

## Results

Of the 8014 PHIV who were in care in the RWP Part A/MAI in 2016 in Miami-Dade County, 1522 (19.0%) excluded for various reasons (Figure 1); 571 of whom were not in care in 2017. Of the 6492 PHIV in the final dataset, 606 (9.4%) were not virally suppressed in 2017.

The majority of the PHIV were >40 years old (65.8%), male (76.3%), and virally suppressed in 2016 (87.5%) (Table 1). In the bivariate analysis, age in 2016, race, Hispanic ethnicity, poverty level, homelessness, problematic alcohol/drug use, feeling depressed or anxious, viral suppression status in 2016, and AIDS status as of 2016 were associated with non-viral suppression in 2017 at  $p < 0.001$ ; whereas food needs, history of injection drug use (IDU), and sex assigned at birth were associated with non-viral suppression in 2017 at  $p < 0.05$ . Transgender status and access to transportation to appointments were not associated with non-viral suppression in 2017.

In the stepwise backward logistic regression model, 12 variables were entered in the initial model, and seven variables maintained statistical significance at  $p$ -value  $< 0.05$ . These risk factors include being in the age group 25-39 ( $\beta = 0.27$ ,  $p < 0.001$ ) or age group

18-24 ( $\beta=0.06$ ,  $p<0.05$ ), Black race  $\beta=0.32$ ,  $p<0.001$ ), poverty level  $<100\%$  ( $\beta=0.17$ ,  $p<0.001$ ), homelessness ( $\beta=0.27$ ,  $p<0.001$ ), problematic alcohol/drug use ( $\beta=0.37$ ,  $p<0.001$ ), diagnosed with AIDS as of 2016 ( $\beta=0.24$ ,  $p<0.001$ ), and not virally suppressed in 2016 ( $\beta=0.91$ ,  $p<0.001$ ) (Table 2). The C-statistic for the derivation model was 0.767% (Figure 2). The optimism-corrected C-statistic was 0.763% (optimism=0.004). The calibration plot shows good calibration with a predicted and observed probability of viral suppression aligning with the 45° line.

The risk score ranged from 0 to 26 (Figure 4). A patient will have highest risk score (score=26) if the patient is aged 25-39, Black, homeless, poverty level $<100\%$ , had AIDS as of 2016, had problematic alcohol/drug use and had unsuppressed viral load in 2016. Non-viral suppression in 2016 greatly predicted non-viral suppression in 2017, and more than one-third of the total risk score was contributed by this variable. The simplified integer-based risk score performed well in the derivation dataset (C-statistic=0.768%). The distribution of predicted and observed percentage by these risk scores is provided in figure 3 (Figure 3). An increase of one point in the risk score was associated with 1.2 increase in the odds of non-viral suppression (OR 1.22; 95 CI, 1.20-1.24).

Figure 4 shows a one-page scoring and decision tool that can be used in health facilities. This scoring and decision tool includes the list of the seven variables and space to record the score for each variable and a total score. On the right side, it includes the risk of non-viral suppression associated with each total score computed from the risk prediction score. To illustrate the application of the risk score, consider a patient who is

27-year-old, Black, has a household poverty level >100%, has permanent housing, has no problematic alcohol/drug use, presents with AIDS diagnosis and has an unsuppressed viral load. Then according to figure 4, the total risk score of the patient can be calculated as 3+3+0+0+0+3+9 which will add up to 18. Looking at the right side of figure 4, this person has a 49.0% probability of not being virally suppressed by the end of next year.

Based on the percentile distribution of the total risk score, we created three categories. These were low risk (score 0–1), medium risk (score 2–7) and high risk (score  $\geq 8$ ). About 15% (n=969) of the study population were in the low risk category, and 1.6% (n=15) of these were not virally suppressed. About 65% (n=4243) of the study population were in medium risk category, of whom 6.0% (n=255) were not virally suppressed. About 20% (n=1280) of the study population were in the high-risk category, and 26.5% (n=339) of these were not virally suppressed. Compared to those who were in the low-risk category, those who were in medium risk and high risk category were more likely not to be virally suppressed (OR 4.06 [CI; 2.40–6.87] and OR 22.89 [CI; 13.54–38.68], respectively).

We estimated sensitivity, specificity and predictive values for various cutoff points in the risk scoring tool. Use of  $\geq 7$  as a risk score cutoff point has a sensitivity of 63%, specificity of 77%, positive predictive value of 21% and negative predictive value of 95%; whereas use of  $\geq 8$  as a cutoff point has a sensitivity of 57%, specificity of 85%, positive predictive value of 31%, and negative predictive value of 94%. Use of  $\geq 9$  as a cutoff point has a sensitivity of 52%, specificity of 88%, positive predictive value of 31%, and negative predictive value of 94%.

## Discussion and Conclusion

We found that non-viral suppression by the end of one-year follow-up time can be predicted using seven variables which are easily ascertained by patient history and medical record. These variables include current age group, race, poverty level, current AIDS diagnosis, current homelessness, problematic alcohol/drug use, and current viral suppression status. The risk prediction tool has a total risk score of 26, and the risk for non-viral suppression increases as the risk score increases. In addition to predicting the magnitude of risk of non-viral suppression associated with each risk score, we also stratified the cohort into risk groups. Those in the high-risk category had about 23 times the risk of having non-viral suppression compared to the low-risk group. The risk prediction tool has good discriminative performance and calibration.

Many studies have identified individual risk factors associated with poor attainment of viral suppression (Crepaz et al., 2018; Whiteside et al., 2014; Sheehan et al., 2017; Joseph Davey et al., 2018; Geter et al., 2018; Castel et al., 2016; Colasanti et al., 2015; Muthulingam et al., 2013; Tanner et al., 2016; Blank et al., 2015; Myers et al., 2016; Beer et al., 2016). Previous studies have shown the predictive role of age group, race, poverty level, AIDS diagnosis, alcohol/drug use, and homelessness on viral suppression (Crepaz et al., 2018; Whiteside et al., 2014; Sheehan et al., 2017; Geter et al., 2018; Castel et al., 2016; Colasanti et al., 2015; Muthulingam et al., 2013; Tanner et al., 2016; Robbins et al., 2010; Powers et al., 2018; Mocroft et al., 2007). Poverty and homelessness may be predictive of viral suppression due to competing needs (Kalichman et al., 2015). AIDS status could affect viral suppression due to advanced nature of the

disease (Langebeek et al., 2014). The predictive role of current viral load to future virologic failure and other HIV disease progression has been demonstrated in previous risk prediction tools (Robbins et al., 2010; Mocroft et al., 2007). There is no evidence of direct mechanism through which race can predict viral suppression. In populations without great disparities in socioeconomic status and access to care such as the military (Silverberg et al., 2009) and populations who receive care from culturally competent healthcare providers (Saha et al., 2013), Black race has not been found to be predictive of HIV care outcomes. In the current study, Black race is likely serving as a proxy for unmeasured factors such as low educational level, stigma, discrimination, mistrust of the health system, and quality of provider relationship that may be differentially affecting the Black PHIV (Centers for Diseases Control and Prevention, 2019; Freeman et al., 2017; Gaston et al., 2013).

Healthcare providers can use different cutoff points depending on availability of resources. If we consider sensitivity and specificity equally important, the cutoff value of 7 in the risk score gave a maximized value of sensitivity and specificity (63% and 77% respectively). The corresponding positive and negative predictive values were 21% and 95%, respectively. However, based on the importance of false-positives and false-negatives, healthcare providers may choose to use different cutoff points. The cutoff point 7 identified 62% of individuals who failed to achieve viral suppression in next year whereas the cutoff point 9 identified 52% of individuals who failed to achieve viral suppression in next year. Moreover, the cutoff point 7 would put 26.8% of our population for intervention whereas the cutoff point 9 would put 15.7% of our population for intervention. A lower cutoff value in the risk score would put a large proportion of our



population into a group to be targeted for intervention and would identify the majority of individuals who failed to achieve viral suppression in next year.

Our study builds on Robbins et al study using more recent data. But our study is different from the Robbins et al study in the definition of the outcome. Robbins et al included patients who were virologically suppressed on ART at enrollment and defined virologic failure as 1) two consecutive measurements of HIV RNA level of  $>400$  copies/mL or 2) one measurement of HIV RNA level of  $>400$  copies/mL and no confirmatory test in the subsequent 3 months (Robbins et al., 2010). In our study, we included all PHIV regardless of viral suppression status, and our outcome of interest, non-viral suppression was defined as having viral load  $\geq 200$  copies/mL in the last viral load measurement of the subsequent year. Moreover, while Robbins et al included factors such as adherence to ART and prior antiretroviral history, which are not available in our dataset, our study considered additional socioeconomic factors such as poverty level, access to transportation to medical appointments, food needs, transgender status and AIDS status to develop the risk prediction model.

We attempted to explore alternative models with a reduced number of predictors (data not shown). After we exclude homelessness from the model, the discriminative performance of the model was similar (C-statistic=0.763). In order to assess the performance of the model in situations where viral load measurement is not available, we excluded viral suppression status in 2016 from the model, but the C-statistic greatly reduced to 0.70.

Risk prediction tools that are simple to use, accurate in predicting risk, and are generalizable across contexts, and use routinely collected variables are needed to identify patients at high risk for poor outcomes and to provide individualized risk assessment (McNairy et al., 2017). The risk prediction tool developed in this study needs external validation to evaluate its performance in other populations. The risk score could be useful in settings similar to the Ryan White Program. When a person with HIV visits an HIV care provider, the provider can quickly and easily use this tool to predict the probability of the person being not virally suppressed by the end of next year. Thus, the scoring can be useful to stratify PHIV into risk categories so that resources are directed to those at greater risk. Accordingly, patients can be targeted for intervention. Depending on the available resources and infrastructure, multi-faceted interventions can be implemented to improve the success of the HIV care continuum. Addressing service-related, medical and psychosocial factors, designing community-based interventions including management and/or patient navigation (Raj et al., 2018), home-based health care, economic empowerment and population specific interventions such as youth friendly clinics and services (Casale et al., 2019; Bulsara et al., 2019) could improve the success of patients in the HIV care continuum.

About 8% (571) of those receiving care in 2016 were not in care in 2017 (lost to follow-up). We compared the baseline characteristics of our study population (those in care in 2017) and those lost to follow-up in 2017. Compared to our study population, those lost to follow-up were more likely to be 25–39 years-old (36.1% vs 29.3%;  $p<0.001$ ), Black (53.9% vs 38.5%;  $p<0.001$ ), non-Hispanic (59.2% vs 42.3%;  $p<0.001$ ), have a household poverty level of  $<100\%$  (58.1% vs 42.0%;  $p<0.001$ ), homeless (13.3%

vs 5.2%;  $p < 0.001$ ), not virally suppressed in 2016 (27.3% vs 12.5%;  $p < 0.001$ ), feel depressed or anxious (19.1% vs 14.8%;  $p < 0.001$ ), and have problematic alcohol/drug use (7.0% vs 2.0%;  $p < 0.001$ ). These differences in baseline characteristics indicate that, those lost to follow-up could have worse viral suppression status compared to our study population.

Despite the strengths of this simple risk prediction score model, there are several limitations that need to be acknowledged. First, we had a large sample size, and the model had good discrimination and calibration in the bootstrapped samples, but the model should undergo external validation to see the performance of the risk prediction model/score in other populations. Our population included mostly low income PHIV and had a high proportion of immigrants especially Latinos; hence the predictive performance of the model/score may differ in a population with different sociodemographic and behavioral characteristics from ours. Second, our study included people with new and existing HIV diagnosis. People with new HIV diagnosis may have different challenges to achieve viral suppression. Therefore, they may need a different risk score. Third, we depended on self-report for feeling depressed or anxious and problematic alcohol/drug use; this may have led to underreporting. Fourth, exposures are measured at any time point in 2016; therefore, there might be differential follow-up time. However, we took the first comprehensive health assessment measurement of 2016 to ensure adequate follow-up time. Last, we were not able to measure adherence to ART and the duration of time the patients had been on ART. Including information about adherence to and duration of patients under ART could have improved the discrimination of the predictive model.

In summary, we have identified a set of readily available variables that can be used to predict non-viral suppression after a year of being in care among PHIV. The predictors of non-viral suppression were age group, race, poverty level, AIDS diagnosis, homelessness, problematic alcohol/drug use, and viral suppression status. The tool has good discriminative ability. Additionally, the tool can be used to stratify PHIV into risk groups that can be identified for targeted intervention. In settings with similar demographics, the risk prediction tool can assist clinicians and healthcare providers to identify high-risk individuals and target for interventions. Follow-up studies are required to externally validate this risk prediction tool.

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Tables and figures

Table 1. Population characteristics of PHIV (N=6492) by viral suppression status and association of factors with non-viral suppression

Characteristics	Total	Virally suppressed n (%)	Not virally suppressed n (%)	Unadjusted OR (95% CI)	p-value
Total	6492	5883 (90.6)	609 (9.4)		
Age (years) in 2016					<0.001
18–24	330	287 (87.0)	43 (13.0)	1.75 (1.25–2.46)	
25–39	1905	1674 (87.9)	231 (12.1)	1.61 (1.35–1.93)	
≥40	4257	3922 (92.1)	335 (7.9)	Ref	
Sex at birth					0.003
Male	4952	4516 (91.2)	436 (8.8)	Ref	
Female	1540	1367 (88.8)	173 (11.2)	1.31 (1.09–1.58)	
Race					<0.001
White/Other	3991	3742 (93.8)	249 (6.2)	Ref	
Black	2501	2141 (85.6)	360 (14.4)	2.53 (2.13–3.00)	
Hispanic ethnicity					<0.001
Yes	3747	3506 (93.6)	241 (6.4)	Ref	
No	2745	2377 (86.6)	368 (13.4)	2.25 (1.90–2.67)	
FPL <100%					<0.001
Yes	2729	2378 (87.1)	351 (12.9)	2.01 (1.69–2.37)	
No	3763	3505 (93.1)	258 (6.9)	Ref	
Homeless					<0.001
Yes	339	265 (78.2)	74 (21.8)	2.93 (2.23–3.85)	
No	6153	5618 (91.3)	535 (8.7)	Ref	
Alcohol/drug use resulted in any problem in daily activity or legal issue or hazardous situation					<0.001
Yes	130	89 (68.5)	41 (31.5)	4.70 (3.21–6.87)	
No	6362	5794 (91.1)	568 (8.9)	Ref	
Are you feeling depressed or anxious?					<0.001

Yes	958	826 (86.2)	132 (13.8)	1.69 (1.38–2.08)	
No	5534	5057 (91.4)	477 (8.6)	Ref	
Getting the food he/she needs					<0.019
Yes	6398	5805 (90.7)	593 (9.3)	Ref	
No	94	78 (83.0)	16 (17.0)	2.01 (1.17–3.46)	
Had CDC-defined AIDS in 2016					<0.001
Yes	2634	2313 (87.8)	321 (12.2)	1.72 (1.46–2.03)	
No	3858	3570 (92.5)	288 (7.5)	Ref	
Virally suppressed in 2016?					<0.001
Yes	5682	5344 (94.0)	338 (6.0)	Ref	
No	810	539 (66.5)	271 (33.5)	7.95 (6.62–9.54)	
History of IDU					0.022
Yes	108	91 (84.3)	17 (15.7)	1.83 (1.08–3.09)	
No	6384	5792 (90.7)	592 (9.3)	Ref	
Has access to transportation to appointments					0.137
Yes	5883	5342 (90.8)	541 (9.2)	Ref	
No	609	541 (88.8)	68 (11.2)	1.24 (0.95–1.62)	
Transgender					0.385
Yes	37	32 (86.5)	5 (13.5)	1.52 (0.59–3.90)	
No	6455	5851 (90.6)	604 (9.4)	Ref	

PHIV: People with HIV; IDU: Injection drug use; FPL: Federal Poverty Level; AIDS: Acquired Immunodeficiency Syndrome; OR: Odds ratio; CI: Confidence Interval; CDC: Centers for Diseases Control and Prevention

Table 2. Final predictors of non-viral suppression and associated risk scoring system

Characteristics	Beta estimate	Score*
Age in 2016		
18-24	0.06	1
25-39	0.27	3
≥40	Ref	0
Race		
White/Other	Ref	0
Black	0.32	3
FPL <100%		
Yes	0.17	2
No	Ref	0
Homeless		
Yes	0.27	3
No	Ref	0
Alcohol/drug use resulted in any problem in daily activity or legal issue or hazardous situation		
Yes	0.37	4
No	Ref	0
Had CDC-defined AIDS in 2016		
Yes	0.24	3
No	Ref	0
Virally suppressed in 2016		
Yes	Ref	0
No	0.91	9

FPL: Federal Poverty Level; AIDS: Acquired Immunodeficiency Syndrome; CDC: Centers for Diseases Control and Prevention

\*Scores are formed by multiplying the beta coefficients by 10 and then rounding to the nearest integer

Figure 1. Flow diagram of exclusion criteria in the present study

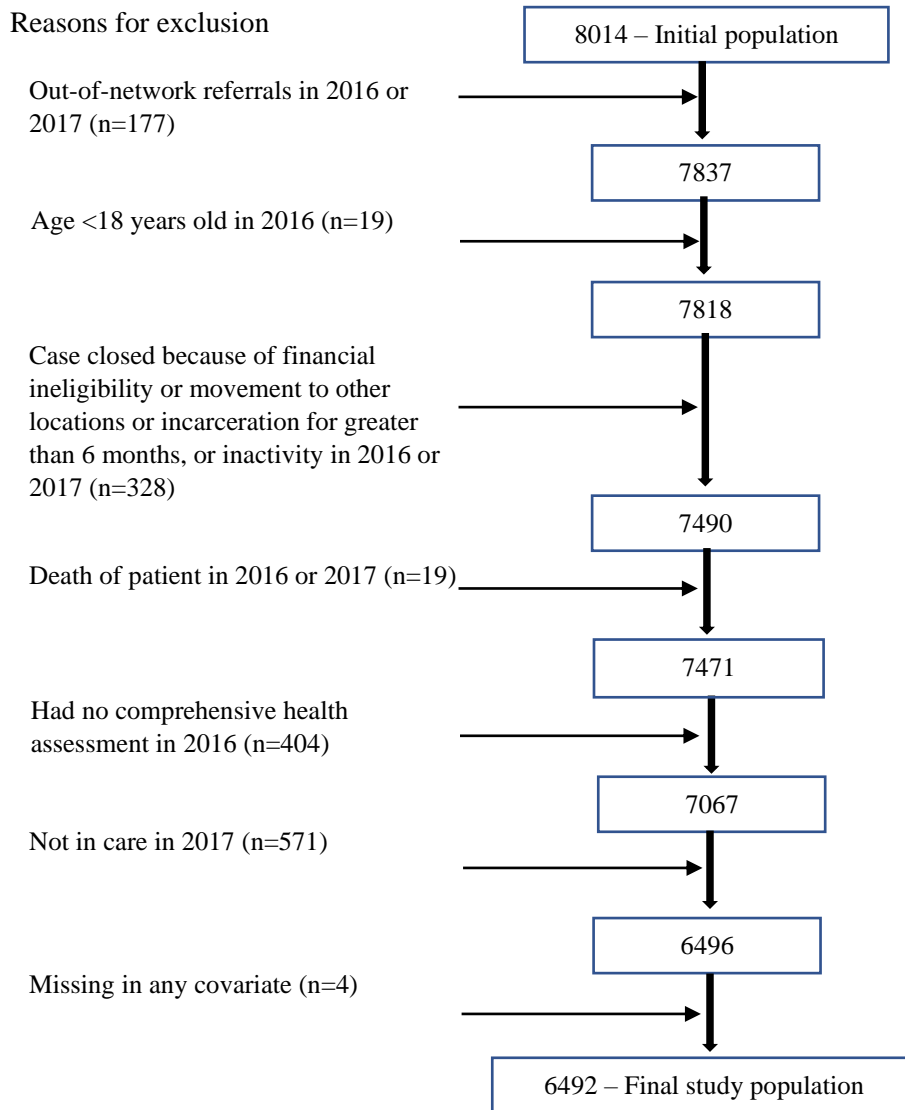


Figure 2. Receiver operating characteristic (ROC) curves for the final logistic regression model

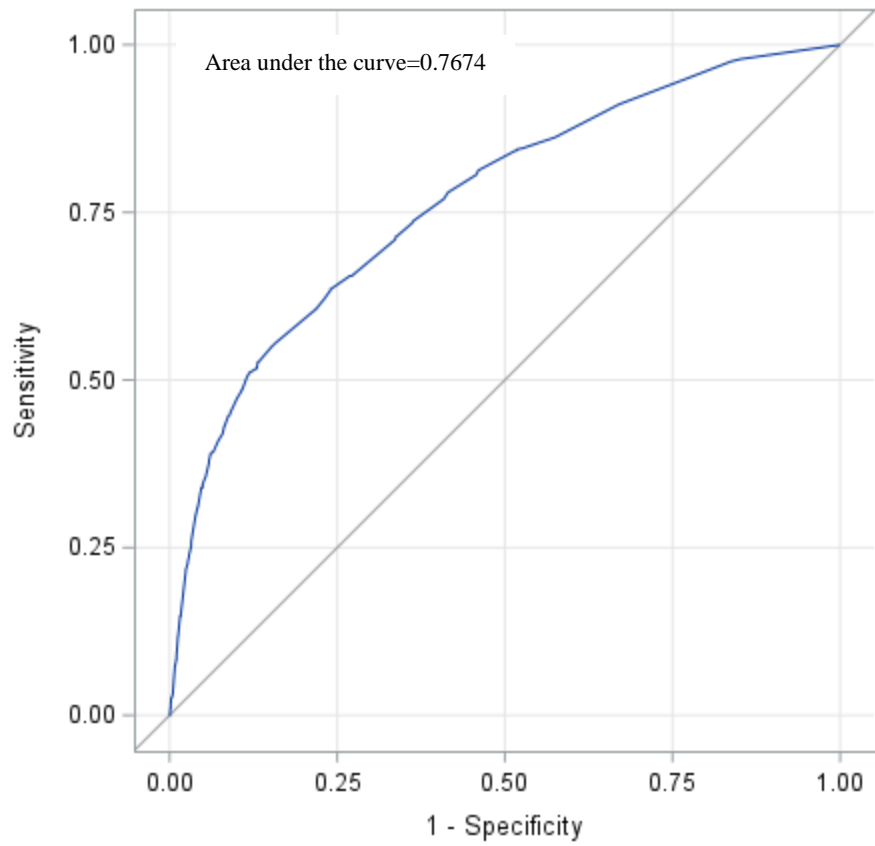


Figure 3. Distribution of predicted and observed percentages by these risk scores

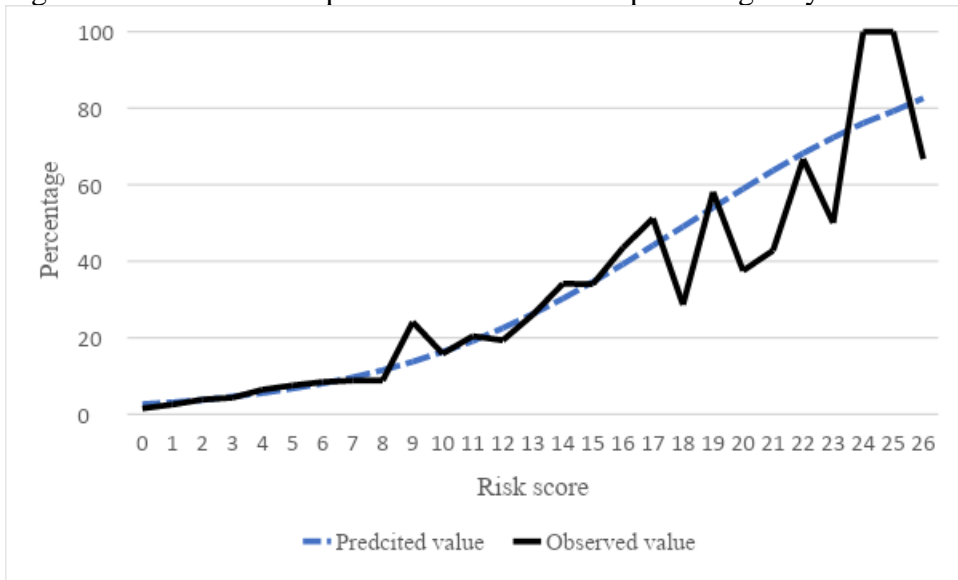


Figure 4. Risk score tool for non-viral suppression after a year of being in care and predicted risks associated with total scores

<u>Risk factor</u>	<u>Score</u>	<u>Patient's score</u>	<u>Risk Score</u>	<u>Predict risk of non-viral suppression (%)</u>
Age in 2016 (years)				
18-24	1			
25-39	3			
≥40	0		0	2.6
Race		_____	1	3.1
Other	0		2	3.7
Black	3		3	4.6
FPL <100%		_____	4	5.5
Yes	2		5	6.7
No	0		6	8.0
Homeless		_____	7	9.6
Yes	3		8	11.5
No	0		9	13.7
Alcohol/drug use resulted in any problem in daily activity or legal issue or hazardous situation		_____	10	16.3
Yes	4		11	19.1
No	0		12	22.5
Had CDC-defined AIDS as of 2016		_____	13	26.2
Yes	3		14	30.2
No	0		15	34.6
Virally suppressed in 2016		_____	16	39.2
Yes	3		17	44.1
No	0		18	49.0
<b>Total score</b>		_____	19	54.0
			20	58.9
			21	63.7
			22	68.2
			23	72.3
			24	76.1
			25	79.2
			26	82.6

**Abbreviations:** FPL: Federal Poverty Level; AIDS: Acquired Immunodeficiency Syndrome

**How to use this tool:** A risk score for each patient can be calculated by adding the scores for each risk factor. For example, if a patient is 27-year-old, Black, FPL>100%, not homeless, has no alcohol/drug use resulted in any problem in daily activity or legal issue or hazardous situation, presents with AIDS diagnosis and unsuppressed viral load, the health care provider can put the following scores in the patient's score column: Age in 2016=3; Race=3; FPL <100%=0; Homeless=0; has no alcohol/drug use resulted in any problem in daily activity or legal issue or hazardous situation=0; Has CDC-defined AIDS as of 2016=3; and Virally suppressed in 2016=9. By adding all these score (3+3+0+0+0+3+9), the total risk score for the patient is 18. Then looking at the risk score and predicted risk columns, a patient with 18 risk scores will have a probability of 49.0% to have non-viral suppression by the end of one-year follow-up.

**Note:** This risk score tool works if there is complete information on all the six factors. If there is missing information on any of these factors, a separate risk score tool is required.

## MANUSCRIPT 3

Gebrezgi M.T., Fennie K.P., Sheehan D.M., ... & Trepka MJ . Predictors of chlamydia or gonorrhea among people with HIV in Miami-Dade County in 2017. Submitted to Journal of Sexually Transmitted Diseases.

### Abstract

**Background:** The aim of this study was to assess prevalence of chlamydia or gonorrhea and factors associated with the diagnosis among 3,578 low-income people with HIV (PHIV) in the Ryan White Program Part A (RWP) in Miami-Dade County, Florida.

**Methods:** We used 2017 calendar year data from the Miami-Dade County RWP to identify sociodemographic, behavioral, and clinical factors associated with a chlamydia or gonorrhea diagnosis using logistic regression.

**Results:** About 49% of the 7,419 PHIV who were  $\geq 18$  years old in active Ryan White care in 2017 reported being screened for chlamydia or gonorrhea. Of those screened, 2.3% were diagnosed with chlamydia, gonorrhea or both, with the highest prevalence among those 18–39 years of age (4.9%) and men who have sex with men (3.1%). In the adjusted model, compared to PHIV  $\geq 40$  years-old, PHIV aged 18–24 and 25–39 years had higher odds of chlamydia or gonorrhea diagnosis (adjusted odds ratio [aOR] 4.36; 95% confidence interval [CI]: 1.76–10.82 and aOR 4.64; 95% CI; 2.66–8.12 respectively). Those with multiple sexual partners in the last 12 months had higher odds of chlamydia or gonorrhea diagnoses (aOR 1.73; 95% CI; 1.07–2.79).



**Conclusions:** Screening rates for chlamydia or gonorrhea are low, relative to CDC guidelines, but prevalence is high. Interventions are needed to increase rates of screening for these STIs. Moreover, targeted behavioral risk reduction techniques are highly recommended among those 18–39 years of age and those who have multiple sexual partners.

**Keywords:** Chlamydia, Gonorrhea, Predictors, Screening, HIV-infected

### Introduction

Some sexually transmitted infections (STIs) are more common among people with HIV (PHIV) compared with the general population without HIV (McClelland et al., 2005). A systematic review conducted in 2011 examining STIs among PHIV in developed and developing countries found that the median prevalence of an STI was 12.4% with the most commonly reported STIs being syphilis (9.5%), gonorrhea (9.5%), chlamydia (5%), and trichomoniasis (18.8%) (Kalichman et al., 2011).

Sexually transmitted infections are risk factors for HIV transmission and susceptibility (Patel et al., 2014). Sexually transmitted infections in PHIV increase the risk of HIV transmission through HIV shedding, HIV replication, increase in viral diversity, and through co-transmission of HIV with STIs (Galvin & Cohen, 2004). Whether symptomatic or asymptomatic, presence of STIs among PHIV facilitates HIV transmission (Kalichman et al., 2011). In addition, a new STI diagnosis may indicate possible risky behaviors such as unprotected sex with an individual with an STI (Golden et al., 2007; Erbelding et al., 2003). The Centers for Diseases Control and Prevention

(CDC) recommends screening PHIV for STIs (syphilis, gonorrhea, chlamydia) at entry into HIV treatment and at least annually thereafter during the course of HIV care (Workowski & Bolan, 2015). CDC further recommends more frequent screening for STIs depending on individual risk behaviors and the local epidemiology of STIs. Despite the CDC recommendations, the rates of testing for STIs among PHIV are low (Flagg et al., 2015; Quilter et al., 2017). Among sexually active PHIV in the Medical Monitoring Project, the proportion tested annually for syphilis was 55%, gonorrhea 23% and chlamydia 24% (Flagg et al., 2015).

Screening for STIs among PHIV is an important component of HIV care, and early diagnosis and treatment of STIs has been suggested to reduce the rates of transmission of HIV. Given the increased prevalence of chlamydia and gonorrhea among PHIV and their risk of transmitting HIV, it is important to identify the associated factors for more targeted management and prevention. Factors such as younger age (Lucar et al., 2018; Ganesan et al., 2012; Rieg et al., 2008; Yang et al 2013; Do et al., 2001), lower educational level (Singa et al., 2013), Hispanic ethnicity (Lucar et al., 2018; Ganesan et al., 2012), men who have sex with men (MSM) ((Lucar et al., 2018; Yang et al 2013; Hu et al., 2014), having more sexual partners (Kalichman et al., 2010), male gender, history of hepatitis (Ganesan et al., 2012), being non-Hispanic Black (Yang et al 2013), fewer than three years since HIV diagnosis, previous STI (Carpenter et al., 2013), higher CD4 cell count, and substance use (Rieg et al., 2008) were found to be associated with STI diagnosis. In this study, the primary objective was to identify additional sociodemographic, behavioral, and clinical factors associated with chlamydia and gonorrhea diagnosis among PHIV in the Ryan White Program in Miami-Dade County.

## Methods

### Population

Miami-Dade County Ryan White Program (RWP) Part A/ Minority AIDS Initiative (MAI) data for the 2017 calendar year were used to identify sociodemographic, behavioral, and clinical factors associated with chlamydia or gonorrhea diagnosis. The RWP is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services to provide comprehensive HIV care, essential support services, and medications for low-income people with HIV who are uninsured and underserved. We included people who had received at least one medical case management encounter or peer education support network service (and who had a medical case manager-administered Comprehensive Health Assessment (CHA), our source of data on screening, diagnoses and patient characteristics) in 2017. We excluded PHIV who were less than 18 years of age in January 2017, out-of-network referrals in 2017 (people who were referred to the RWP from a non-RWP provider for ancillary services only, and would, therefore, have no CHA) and those who died in 2017. We also excluded people whose case was closed due to moving to another state/county, financial ineligibility, or incarceration for greater than 6 months in 2017. Moreover, we excluded people who had missing information on covariates (37 people had missing information on sustained viral load suppression).

## Independent variables, and outcome of interest

Our independent sociodemographic, behavioral, and clinical factors were obtained from the patients' self-reported CHA data, collected at time of entry into the RWP and bi-annually thereafter, and from laboratory results entered into the client's electronic case management file (Table 1). A description of the sociodemographic, behavioral, and clinical factors included in the analysis is given in Table 1. The annual chlamydia or gonorrhea screening rate was obtained from the self-reported CHA (screened for chlamydia in 2017 (yes/no) and screened for gonorrhea in 2017 (yes/no)). The outcome of interest, chlamydia or gonorrhea diagnosis during the year 2017, was drawn from the self-reported chlamydia and gonorrhea screening results on the CHA. A client was considered to have a diagnosis of chlamydia or gonorrhea if he/she self-reported any positive result during either of the bi-annual CHA interviews.

## Data Analysis

We calculated annual chlamydia or gonorrhea screening rates for 2017 as the number of RWP clients who reported receiving at least one test for chlamydia or gonorrhea in 2017 (3578) divided by all PHIV 18 and over years old who are actively enrolled in the RWP in the same year (7419). We calculated prevalence of chlamydia or gonorrhea as the number of people who reported at least one positive result for chlamydia or gonorrhea divided by the number of people who were screened in 2017. We conducted descriptive analyses for the prevalence of chlamydia or gonorrhea to provide percentages and frequencies of key parameters. Variables which were significant at  $p < 0.1$  in the bivariate analysis were kept for the multivariable analysis. We estimated unadjusted and

adjusted odds ratios with 95% confidence intervals (CI) to evaluate the association between socioeconomic, behavioral and clinical factors and chlamydia or gonorrhea diagnosis using a logistic regression model. All analyses were conducted using SAS software V. 9.4 (SAS Institute Cary, NC).

### Ethical Approval

This study was approved by Florida International University Institutional Review Board.

### Results

Of those 7419 PHIV actively enrolled in case management in the RWP in 2017, a total of 3578 (48.7%) reported being screened for chlamydia or gonorrhea. The mean age of the screened population was 44 years (SD 11.14). The majority of the participants were males (82.3), foreign born (72.5%), Hispanic (65.7%), household income  $\geq 100\%$  of the Federal Poverty Level (FPL) (65.2%), and  $\geq 40$  years of age (63.1%), (Table 2). Of those screened, 82 (2.3%) reported at least one positive test for chlamydia or gonorrhea. Of those, 39 had chlamydia only, 33 had gonorrhea, and 10 had both. All gonorrhea cases were reported among males. The highest percent of chlamydia or gonorrhea was reported among people who reported problematic alcohol use (7.0%), were aged 18–39 (4.9%), had more than one sexual partner in the last 12 months (4.6%), reported unprotected sex (3.8%), and were MSM (3.1%).

In the bivariate analysis (Table 2), chlamydia or gonorrhea diagnoses were significantly associated with being aged 18–39 (p-value  $< 0.001$ ), being male (p-value

<0.05), being men who have sex with men (p-value <0.05), not self-identifying as Haitian (p-value <0.05), living alone (p-value <0.05), not being diagnosed with AIDS as of 2017 (p-value <0.05), reporting problematic alcohol use (p-value <0.05), being sexually active (p-value <0.05), reporting more than one sexual partner in the last 12 months (p-value <0.001), and reporting unprotected sex (p-value <0.05). In a full of model containing variables that were significantly associated with chlamydia or gonorrhea in bivariate analyses, age group and having more than one sexual partner in the last 12 months were significantly associated with chlamydia or gonorrhea diagnoses (Table 3). Compared to those aged 40 years and older, those aged 18–24 and those aged 25–39 were more likely to report chlamydia or gonorrhea diagnosis (adjusted odds ratio [aOR] 4.36; 95% confidence interval [CI]: 1.76–10.82 and aOR 4.64; 95% CI; 2.66–8.12 respectively). Those who had more than one sexual partner during the last 12 months had higher odds of chlamydia or gonorrhea diagnosis report (aOR 1.73; 95% CI; 1.07–2.79) compared to those who did not.

## Discussion and Conclusion

In this study, we report factors associated with a chlamydia or gonorrhea diagnosis among a cohort of PHIV in the RWP Part A/MAI in Miami Dade County. Results indicate that, of those enrolled in the RWP in 2017, less than half (48.7%) were screened for chlamydia or gonorrhea. Of those screened for chlamydia or gonorrhea, 2.3% were diagnosed with chlamydia or gonorrhea, or both, with the highest prevalence being among those 18–39 years of age and those who are MSM. We found that being

aged 18–24, aged 25–39, and having multiple sexual partners in the last 12 months were significant predictors of chlamydia or gonorrhea diagnosis reports.

Although the primary objective of this study was to assess the predictors of chlamydia or gonorrhea diagnosis, we also estimated chlamydia or gonorrhea screening to improve our understanding of the findings. Our results were consistent with findings of previous studies (Flagg et al., 2015; Quilter et al., 2017), receipt of chlamydia or gonorrhea screening was found to be suboptimal in our study. CDC recommends screening sexually active individuals, at first HIV evaluation, and at least annually thereafter during the course of HIV care (Workowski & Bolan, 2015). Previous studies found that health care providers adhere to recommendations for syphilis screening but conduct suboptimal chlamydia and gonorrhea screening (Carter et al., 2014; Barbee et al., 2015).<sup>21,22</sup> Obstacles that prevent routine chlamydia and gonorrhea screening may include time constraints, difficulty obtaining a sexual history, language and cultural barriers, patient confidentiality, patient reluctance, lack of comfort discussing sexual history with provider and concerns about provider judgment (Quilter et al., 2017; Carter et al., 2014; Barbee et al., 2015). Interventions, such as adoption of standard STI testing protocols, promoting culturally sensitive risk assessment skills and tools, patient-driven health service models that promote self-assessment, and creating an alert system in electronic medical records may increase the proportion of people screened for STI (Flagg et al., 2015; Barbee et al., 2015).

Prevalence of STIs is increasing in the general population (Centers for Disease Control and Prevention, 2018) and among PHIV (Taylor et al., 2013; Skinner et al.,

20140. In our study, about 2% of those screened were positive for either chlamydia or gonorrhea, and 10 (12%) of those screened had both chlamydia and gonorrhea. The prevalence of chlamydia or gonorrhea in our study is high compared to the prevalence in the general population, but it is low compared to other studies conducted among PHIV. In District of Columbia, during a median follow-up time of 32.5 months, Lucar et al found 4% of participants were diagnosed with chlamydia, and 3% were diagnosed with gonorrhea (Lucar et al., 2018). In our study, high risk groups might not be screened, or patients might not have reported chlamydia or gonorrhea test results diagnosed elsewhere as reported in another study (Whitlock et al., 2011). Moreover, chlamydia or gonorrhea diagnosis was self-reported, and the prevalence might be underestimated due to recall bias or social desirability bias. Patients may also be reluctant to report STI diagnosis or may be afraid to share the information. Florida law requires people with HIV and STI to disclose their HIV status to their sexual partners (The Center for HIV Law and Policy, n.d). The law declares that, “It is unlawful for any person who has chancroid, gonorrhea, granuloma inguinale, lymphogranuloma venereum, genital herpes simplex, chlamydia, nongonococcal urethritis (NGU), pelvic inflammatory disease (PID)/acute salpingitis, or syphilis, when such person knows he or she is infected with one or more of these diseases and when such person has been informed that he or she may communicate this disease to another person through sexual intercourse, to have sexual intercourse with any other person, unless such other person has been informed of the presence of the sexually transmissible disease and has consented to the sexual intercourse (The Center for HIV Law and Policy, n.d).”



In agreement with previous studies (Lucar et al., 2018; Carpenter et al., 2013), after controlling for covariates, our study found higher odds of chlamydia or gonorrhea diagnosis among PHIV aged 18–39 and those having multiple sexual partners in the last 12 months. Problematic alcohol use was significant in the bivariate analysis, but the association was attenuated in the multivariate analysis. Contrary to our expectation, being MSM was not a significant predictor of chlamydia or gonorrhea diagnosis in our study, although prevalence was high in this group. This likely may explain the inclusion of more proximal determinants of STI in our model such as number of sexual partners. To test for the presence of more proximal factors in our model, we conducted a post-hoc analysis. After we excluded being sexually active and having more than one sexual partner from the model, being MSM became significant at  $p$ -value  $<0.05$ . Thus, sexual activity might be explaining the pathway through which MSM predicts chlamydia or gonorrhea diagnosis. Our results didn't show any significant association between sustained viral suppression and prevalence of chlamydia or gonorrhea. People with HIV who are on ART and have a sustained viral load may perceive that they have lower risk of HIV or STI transmission and may increase their risky sexual activity (Ostrow et al., 2002). Contrary to this hypothesis, sustained viral suppression was not significantly associated with chlamydia or gonorrhea infection in our bivariate and multivariate analysis. We conducted bivariate analysis for the predictors of chlamydia and gonorrhea diagnosis separately. The association between sociodemographic, behavioral, and clinical factors and each outcome was similar except for problematic alcohol use. Problematic alcohol use was significant for gonorrhea diagnosis ( $p$ -value $<0.05$ ) but not for chlamydia diagnosis. We had insufficient sample size to test for the association among other factors.

There are limitations to consider when interpreting our findings. First, our study depended on self-reported chlamydia or gonorrhea diagnosis among PHIV and thus may be underreported. But studies have shown that self-reported STI diagnosis is a reliable measure (Niccolai et al., 2005; Fisher et al., 2007). Second, the screening rate for chlamydia or gonorrhea in 2017 was also self-reported. The rate may be underreported because patients may not be informed about STI screenings when a doctor conducts the annual screening. Third, we were not able to conduct stratified analyses by sex assigned at birth because we had insufficient numbers of chlamydia or gonorrhea diagnoses among females. But in a post-hoc analysis, we assessed the sociodemographic, behavioral and clinical predictors of chlamydia or gonorrhea diagnosis among males. The results of the final model were similar to the results of the final multivariate model among the general population. Fourth, our analysis didn't include significant proximate predictors of STIs such as participants' sexual networks, levels of alcohol used, and alcohol/drug use before or during sex. These factors could be better predictors of chlamydia or gonorrhea diagnosis. Finally, our measurements for sexual activity ("Are you sexually active?") and depression/anxiety ("Have you been feeling depressed or anxious?") are subjective measurements, and validated scales were unavailable in the dataset.

In summary, our results highlight the importance of regular screening among PHIV. Screening for chlamydia or gonorrhea is suboptimal and prevalence is high among PHIV. People aged 18–24 and 25–39 and those who have multiple sexual partners in the last 12 months had increased chlamydia or gonorrhea diagnosis. Therefore, there is a need for targeted behavioral risk reduction techniques among those groups to reduce STI

transmission and subsequently HIV transmission. In addition, interventions are required to increase the proportion of population screened for chlamydia or gonorrhea.

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Tables and figures

Table 1. Operational definition and categorization of variables

Name of variable	Definition and/or categorization
Age in 2017	18–24, 25–39 and $\geq 40$ years
Sex assigned at birth	Male, Female
Men who have sex with men	Yes, No
United States born	Yes, No
Race	Black, White/other Other includes Asian, Native American/Alaskan Native, Native Hawaiian/Pacific Island
Hispanic ethnicity	Yes, No
Haitian	Yes, No
Federal poverty level (FPL) <100%	Yes, No Federal poverty level <100% was defined as having a household income less than \$11,880 for a single person. <sup>19</sup>
Currently working	Yes, No
Household size	1=One person, 2=More than one person
Homelessness	Yes, No A person was categorized as homeless if he/she reported a non-permanent (includes homeless, transient, or transitional) living arrangement
CDC-defined AIDS status as of 2017	Yes, No
Sustained viral load in 2017	Yes, No Sustained viral suppression was defined as having a HIV viral load <200 copies/ml in all viral load tests in 2017. For people who had only 1 viral load measurement in 2017 (or had at least 2 viral load measurements less than 3 months apart) and the test showed viral suppression, we included the last viral load test in 2016 in an effort to assess consistent viral load suppression on at least 2 tests. <sup>20</sup>
Do you smoke?	Yes, No
History of injection drug use (IDU)	Yes, No A patient was considered to have a history of IDU if (a) he/she has responded “Yes” to the question “Have you ever injected drugs?” Or (b) reported “IDU” or “IDU and male to male sexual intercourse” as mode of HIV transmission.
Problematic alcohol/drug use resulting in any problem in daily activity or legal issue or hazardous situation	Yes, No Problematic alcohol/drug use was derived from three questions namely; (a) Has alcohol/drug use resulted in hazardous situation, (b) Has alcohol/drug use resulted in legal problems (c) Is your alcohol/drug use preventing you from carrying out your daily activities?

Feeling depressed or anxious?	Yes, No Feeling depressed or anxious was assessed based on a question: "Have you been feeling depressed or anxious?"
Do you have a partner?	Yes, No
Are you sexually active?	Yes, No
Having more than one sexual partner in the last 12 months	Yes, No
Do you use protection during sexual intercourse?	Yes, No Those who have never used protection and those who sometimes use protection were categorized as "No," whereas those who didn't report any sexual activity, or those who reported to use protection always, were categorized as "Yes".

Table 2. Distributions of socioeconomic, behavioral and clinical factors and their relationships with chlamydia or gonorrhea diagnoses among PHIV who reported chlamydia or gonorrhea screening in the Ryan White program in Miami-Dade County in 2017 (N=3578)

Characteristics	Total population N 3578	Positive for chlamydia or gonorrhea		p-value*
		Yes n (%) 82 (2.3)	No n (%) 3533 (97.7)	
Age in 2017				<0.001
18–24	151	7 (4.6)	144 (95.4)	
25–39	1168	57 (4.9)	1111 (95.1)	
≥40	2259	18 (0.8)	2241 (99.2)	
Sex assigned at birth				<0.05
Male	2945	77 (2.6)	2866 (97.4)	
Female	635	5 (0.8)	630 (99.2)	
Men who have sex with men				<0.001
Yes	2301	71 (3.1)	2230 (96.9)	
No	1277	11 (0.9)	1266 (99.1)	
US born				0.173
Yes	984	28 (2.8)	956 (97.2)	
No	2594	54 (2.1)	2540 (97.9)	
Race				0.188
White/other**	2514	63 (2.5)	2451 (97.5)	
Black	1064	19 (1.8)	1045 (98.2)	
Hispanic ethnicity				0.453
Yes	2351	57 (2.4)	2294 (97.6)	
No	1227	25 (2.0)	1202 (98.0)	
Haitian ethnicity				<0.05
Yes	311	2 (0.6)	309 (99.4)	
No	3267	80 (2.5)	3187 (97.5)	
Federal poverty level <100%				0.901
Yes	1245	28 (2.3)	1217 (97.8)	
No	2333	54 (2.3)	2279 (97.7)	
Currently working				0.110
Yes	2391	61 (2.5)	2330 (97.5)	
No	1224	21 (1.7)	1203 (98.3)	
Household size				<0.05
1 person	2938	77 (2.6)	2861 (97.4)	
>1 person	640	5 (0.8)	635 (99.2)	
Homeless				0.447
Yes	146	2 (1.4)	144 (98.6)	
No	3432	80 (2.3)	3352 (97.7)	
CDC-defined AIDS as of 2017				<0.05
Yes	1227	15 (1.2)	1212 (98.8)	
No	2351	67 (2.8)	2284 (97.2)	
Sustained viral load				0.929
Yes	536	12 (2.2)	524 (97.8)	
No	3042	70 (2.3)	2972 (97.7)	



Smoking				0.663
Yes	449	9 (2.0)	440 (98.0)	
No	3129	73 (2.3)	3056 (97.7)	
History of injection drug use				0.617
Yes	137	4 (2.9)	133 (97.1)	
No	3441	78 (2.3)	3363 (97.7)	
Problematic alcohol use				<0.05
Yes	57	4 (7.0)	53 (93.0)	
No	3521	78 (2.2)	3443 (97.8)	
Feeling depressed/anxious				0.970
Yes	485	11 (2.3)	474 (97.7)	
No	3093	71 (2.3)	3022 (97.7)	
Have a partner				0.529
Yes	1450	36 (2.5)	1414 (97.5)	
No	2128	46 (2.2)	2082 (97.8)	
Sexually active				<0.05
Yes	2437	69 (2.8)	2368 (97.2)	
No	1141	13 (1.1)	1128 (98.9)	
Had more than one sexual partner in the last 12 months				<0.001
Yes	884	41 (4.6)	843 (95.4)	
No	2694	41 (1.5)	2653 (98.5)	
Unprotected sex				<0.05
Yes	3181	67 (2.1)	3114 (97.9)	
No	397	15 (3.8)	382 (96.2)	

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US: United States; CDC: Centers for Diseases Control and Prevention; AIDS: Acquired Immune Deficiency Syndrome

\*p-values for the Chi-square test or Fisher exact test

\*\*Other includes Asian (11), Native American/Alaskan Native (6), Native Hawaiian/Pacific Island (3)

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Table 3 Unadjusted and adjusted odds ratio for the association between socioeconomic, behavioral and clinical factors, and chlamydia or gonorrhea diagnosis

Characteristics	Unadjusted OR	Adjusted OR	p-value*
Age in 2017			<0.001
18–24	6.05 (2.49–14.72)	4.36 (1.76–10.82)	
25–39	6.39 (3.74–10.90)	4.64 (2.66–8.12)	
≥40	Ref	Ref	
Sex assigned at birth			0.923
Male	3.38 (1.36–8.40)	1.06 (0.32–3.52)	
Female	Ref	Ref	
Men who have sex with men			0.249
Yes	3.66 (1.93–6.94)	1.68 (0.70–3.91)	
No	Ref	Ref	
US born			
Yes	1.38 (0.87–2.19)	–	
No	Ref	–	
Race			
White/other	Ref	–	
Black	0.71 (0.42–1.19)	–	
Hispanic ethnicity			
Yes	Ref	–	
No	0.84 (0.52–1.35)	–	
Haitian			0.665
Yes	0.26 (0.06–1.05)	0.72 (0.17–3.14)	
No	Ref	Ref	
Federal poverty level			
<100%			
Yes	0.97 (0.61–1.54)	–	
No	Ref	–	
Currently working			
Yes	Ref	–	
No	0.68 (0.41–1.12)	–	
Household size			0.176
1 person	3.42 (1.38–8.48)	1.93 (0.74–5.00)	
>1 person	Ref	Ref	
Homeless			
Yes	0.58 (0.14–2.39)	–	
No	Ref	–	
CDC-defined AIDS as of 2017			0.406
Yes	0.42 (0.24–0.74)	0.78 (0.43–1.41)	
No	Ref	Ref	
Sustained viral load			
Yes	Ref	–	
No	1.03 (0.55–1.91)	–	
Smoking			
Yes	0.86 (0.43–1.72)	–	
No	Ref	–	

History of injection drug use				
Yes	1.30 (0.47–3.60)	–		
No	Ref			
Problematic alcohol use				0.077
Yes	3.33 (1.18–9.43)	2.67 (0.90–7.96)		
No	Ref	Ref		
Feeling depressed/anxious				
Yes	0.99 (0.52–1.88)	–		
No	Ref	–		
Have a partner				
Yes	Ref	–		
No	0.87 (0.56–1.35)	–		
Sexually active				0.158
Yes	2.53 (1.39–4.59)	1.58 (0.84–3.00)		
No	Ref	Ref		
Had more than one sexual partner in the last 12 months				<0.05
Yes	3.15 (2.03–4.89)	1.73 (1.07–2.79)		
No	Ref	Ref		
Unprotected sex				0.634
Yes	Ref	Ref		
No	1.83 (1.03–3.23)	0.86 (0.47–1.59)		

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US: United States; CDC: Centers for Diseases Control and Prevention; AIDS: Acquired Immune Deficiency Syndrome

\*p-values for the Wald Chi-square test of the multivariate model

The multivariate model included factors related to the outcome at  $p < 0.1$

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## CONCLUSIONS

In this dissertation project, we developed risk prediction tools to identify PHIV who are at risk of non-retention in HIV care and non-viral suppression; and identified predictors of chlamydia or gonorrhea among PHIV.

The first study developed a risk prediction tool to identify PHIV at risk of non-retention in care (defined as having evidence of at least two occurrences of any combination of (a) face-to-face encounter(s) with a Ryan White Program medical care professional, or (b) laboratory tests (CD4 or viral load), at least three months apart during the follow-up year). We found that about 24% of the population were not retained in care in the follow-up year. The risk prediction tool included six factors: age group, race, poverty level, homelessness, problematic alcohol/drug use and viral suppression status. The risk prediction tool had a total score ranging 0 to 17. A cutoff value of 5 in the risk score had a sensitivity of 38% and a specificity of 84%. Moreover, those who were in the high risk (fourth quartile) were about 5 times as likely not to be retained in care compared with those who were in the low risk (first quartile).

The risk prediction tool for non-retention in care had low discrimination (c-statistic=0.65). In order to improve the discrimination, future risk prediction tools should include better predictive factors in the model. Although they may not be routinely accessible, information about factors such as sexually transmitted infections, adherence to medications, prior treatment failure, previous appointment attendance, and other unmet needs could improve discrimination of the model. This risk prediction tool can be used in situations where these additional variables are not available.

The second study developed a risk prediction tool for PHIV who are at risk of not achieving viral suppression (defined as having viral load  $\geq 200$  copies/mL in the last viral load measurement in the follow-up year). About 9% of the population was not virally suppressed in the follow-up year. The risk prediction tool for non-viral suppression included seven factors: age group, race, poverty level, AIDS diagnosis, homelessness, problematic alcohol/drug use, and viral suppression status. The risk prediction tool had good discriminative ability (c-statistic=0.77) and a total score ranging 0 to 26. A cutoff point of 7 in the risk score had a sensitivity of 63%, specificity of 77%, positive predictive value of 21% and negative predictive value of 95%. The cutoff point 7 identified 62% of individuals who failed to achieve viral suppression in next year by putting 26.8% of our population for intervention. Based on the distribution of the total risk score, those in the high-risk category (score 8-26) had about 23 times the risk of having non-viral suppression compared to the low-risk (score 0-1) group. The tool needs external validation in order to assess the performance of the model in other populations.

The factors included in the risk prediction tools can be easily obtained from medical records or by interviewing the patient and can be implemented in a variety of settings. Most of the factors in both risk prediction tools are similar, except the risk prediction tool for non-viral suppression additionally includes the factor AIDS diagnosis. Being diagnosed with AIDS could be a risk factor for being non-viral suppression due to the advanced stage of the disease.

We created an easy-to-use tool for both outcomes. The tools include the risk factors with their corresponding risk scores. The tool also includes the probabilities

associated with each total risk score. Clinicians and healthcare providers can use these tools to calculate the total risk score and the corresponding risk of non-retention in care or non-viral suppression of a patient. These risk prediction tools can identify high-risk individuals who could benefit from any available interventions.

The third study assessed the prevalence of self-reported chlamydia or gonorrhea and factors associated with these self-reported diagnoses among PHIV. We found that about 49% of the PHIV reported that they were screened for chlamydia or gonorrhea during 2017. Relative to the CDC recommendations, this screening rate is low. Of those screened, 2.3% reported that they were diagnosed with chlamydia, gonorrhea or both. The highest prevalence of chlamydia or gonorrhea was among those 18–39 years of age (4.9%) and men who have sex with men (3.1%). In the multivariate model, compared to those  $\geq 40$  years-old, those 18–39 years-old had higher odds of self-reported chlamydia or gonorrhea diagnosis. Moreover, those who had multiple sexual partners in the last 12 months had increased odds of chlamydia or gonorrhea diagnosis. Our results highlight the importance of interventions to increase the proportion of population screened for chlamydia or gonorrhea. Moreover, targeted behavioral risk reduction techniques are recommended for those 18–39 years of age and those who have multiple sexual partners to reduce STI transmission and subsequently HIV transmission.

## VITA

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### PUBLICATIONS AND POSTERS/PRESENTATIONS (Selected)

- Gebrezgi M.T., Fennie K.P., Sheehan D.M., ... & Trepka MJ. (2020). Developing a triage tool for use in identifying people living with HIV who are at risk for non-retention in HIV care. *Int J STD AIDS*. In press.
- Gebrezgi M.T., Fennie K.P., Sheehan D.M., ... & Trepka MJ. (2020). Development and validation of a risk prediction tool to identify people living with HIV likely not to achieve viral suppression. *AIDS Pt Care and STDs*. In press.
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