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Factors Associated with Progression towards HIV Viral Suppression and Sexual Behavior Change among the Framework of the HIV Care Continuum

Author

Chien, Michael

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Factors Associated with Progression towards HIV Viral Suppression and Sexual Behavior Change among the Framework of the HIV Care Continuum

A dissertation submitted in partial satisfaction of the requirements

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by

Michael Wei-Chau Chien

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ABSTRACT OF THE DISSERTATION

Factors Associated with Progression towards HIV Viral Suppression and Sexual Behavior Change among the Framework of the HIV Care Continuum

by

Michael Wei-Chau Chien

Doctor of Philosophy in Epidemiology

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Frank J. Sorvillo, Chair

Currently, the most effective method to reduce further transmission and optimize the well-being of those with HIV is to achieve and maintain viral suppression. The HIV Care Continuum is commonly used as a framework to monitor progress towards this end goal. As such, it is important to understand the dynamics of progressing through each stage of the continuum in order to implement effective targeted interventions.

This study was, to the best of our knowledge, the first to evaluate a cohort of HIV-positive individuals through the entire course of the HIV care continuum: from diagnosis through viral suppression. Thus, factors associated with overall viral suppression and progression to each intermediate continuum stage could be evaluated within the same population, allowing for a more standardized comparison of the relevant determinants between the stages. This type of

comparison was lacking in the current literature, in which information about the continuum stages must be derived from different studies based on different study populations.

As such, our study (Chapter 2) was able to evaluate associations at each continuum stage and provide insight into the consistency of these associations throughout the continuum. We observed that certain factors associated with overall viral suppression were not always significant at every stage. Conversely, some factors that were associated with a certain intermediate stage were not associated with overall viral suppression. For example, race/ethnicity was significantly associated with viral suppression among everyone diagnosed. However, there was no difference between the ethnic groups with regards to linkage and retention. Therefore, within this population, interventions and policies aimed towards increasing linkage/retention in these ethnic groups in hopes of improving viral suppression rate would be misdirected and ineffectual. Our results demonstrate the importance of understanding the continuum as a whole in any given population to best direct public health resources.

Another aspect relevant to the appropriateness of the HIV care continuum is the designated definitions of the intermediate stages. The intermediate stage with the most variation in definition is retention in care. For any given population, any retention measure used must be significantly associated with increased viral suppression (among the retained). However, another perhaps more clinically practical perspective in deciding the most appropriate retention measure definition would be determining the measure that best predicts viral suppression. This study (Chapter 3) was also the first to evaluate eight different measures of retention, with measures involving kept visits, missed visits, and HIV laboratory tests, among a single population. Further, our study was among the few to apply a non-traditional statistical-learning method (k-folds cross validation) to estimate the accuracy of the retention measures in predicting viral

suppression among new patients. The results demonstrated that although no gold standard retention measure may exist, each retention measure evaluated was significantly associated with increased viral suppression as well as positive predictor of viral suppression. However, the difference between the ranking of strength of association (odd ratio) and predictive accuracy (from cross-validation) indicates that traditional statistical methods alone may not best determine prognostic ability of the measures. Methods such as those in statistical learning can be utilized in evaluating the most appropriate measure for each population.

Aside from viral suppression, another goal of HIV counseling and care is to reduce the sexual behaviors that promote transmission. The literature is mixed with regards to the direction of change in high-risk sexual behaviors at different points after HIV diagnosis: 1) following linkage to care; and 2) following initial viral suppression. Our analyses (Chapter 4) also evaluated the direction of any change in sexual behavior at these two time points using STD incidence as a proxy. The results provided more support for an attenuation in high-risk behavior possibly related to treatment adherence than for an increase due to "HAART complacency". In addition, the findings were more consistent with a reduction in high-risk behaviors observed following HIV diagnosis. Ethnicity was also associated with reduction in STD incidence. Further sub-analysis based on the association with ethnicity revealed a subgroup of clients that were at potentially high-risk for HIV transmission (no reduction in high-risk sexual behavior, concurrent STD infection, and less likely to be virally suppressed). Future studies and programs should focus on identifying these high-risk subgroups in addition to the broader analyses on sexual behavior change.

The dissertation of Michael W. Chien is approved.

Marjan Javanbakht

Sung-Jae Lee

Warren S. Comulada

Frank J. Sorvillo, Committee Chair

University of California, Los Angeles

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LIST OF ABBREVIATIONS

AHF	AIDS Healthcare Foundation
AIDS	Acquired Immune Deficiency Syndrome
AOR	Adjusted Odds Ratio
ART	Antiretroviral Therapy
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CV	Cross-validation
HIV	Human Immunodeficiency Virus
HRSA	Health Resources and Services Administration
MSM	Men Who Have Sex With Men
NCQA	National Committee for Quality Assurance
OR	Odds Ratio
STD	Sexually Transmitted Disease
VL	Viral Load
VS	Viral Suppression

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VITA

1996	B.A., Integrative Biology
	University of California, Berkeley
	Berkeley, CA
2000	M.P.H., Epidemiology
	Loma Linda University, School of Public Health
	Loma Linda, CA

ABSTRACTS AND PRESENTATIONS

- **Chien, Michael**, et al. STD Co-infection Among Acute HIV Patients in Los Angeles County. Oral Presentation at National STD Prevention Conference; Chicago, Illinois 2008.
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CHAPTER 1

BACKGROUND

1.1 HIV/AIDS Epidemic

The human immunodeficiency virus (HIV) targets and depletes CD4-positive lymphocytes and degrades the overall immune response to infection. Left to its natural course, a HIV infection in the majority of individuals will result in the eventual onset of acquired immunodeficiency syndrome (AIDS) within 8 to 10 years followed by subsequent death from a secondary infection.[1] The first documented cases of HIV in the United States were reported in Los Angeles in 1981.[2] These were followed by additional reported cases in New York and San Francisco.[3] The incidence of HIV in the United States would continue to rise with a probable peak in the mid 80's. The epidemic of AIDS would follow a similar course with a peak in 1993.[4] Since the start of the epidemic in 1981, an estimated 1.8 million people have been infected with HIV in the United States with 667,000 reported AIDS-related deaths.[5] In the United States alone, over 42,000 people are estimated to be newly infected with HIV per year in addition to over 930,000 people already living with HIV. Amongst those living with HIV, over 20,000 are progressing to stage 3 (AIDS) each year.[6] Worldwide, the number of people living with HIV is estimated at 35 million with 1.2 million AIDS-related deaths in 2014 alone.[7]

The demographics of the HIV epidemic in the United States have evolved over time. At the start of the epidemic, the HIV cases were discovered mostly in men who have sex with men (MSM) and injection drug users (IDU). The earliest reported HIV cases from Los Angeles, San Francisco and New York were all MSM. Currently, the majority of the new HIV infections in the United States still occur through male-to-male sexual contact (approximately 80%).

However, heterosexual contact now accounts for almost 10% of new HIV transmissions. In addition, transmissions occurring through intravenous drug use (IDU) currently comprise approximately 5% of new HIV infections. The World Health Organization defines MSM, IDU, together with sex workers and transgendered people as the most at-risk populations.[8] With regards to race/ethnicity, Blacks and Hispanics remain disproportionately affected by the HIV epidemic accounting for 55% and 28% of new HIV infections, respectively.[6] Internationally, the primary drivers of HIV epidemics may differ by region.[9-11]

1.2 HIV Treatment

Therapies to treat HIV infections have improved with increased understanding of HIV biology. Early therapies involved strict multiple-dosing regimens with adverse side-effects. Zidovudine (ZDV or AZT), a reverse-transcriptase inhibitor, was among the first therapies approved by the Food and Drug Administration in 1987.[12] Other types of reverse-transcriptase inhibitors followed and demonstrated only limited success in suppressing HIV viral load. Monotherapy or treatment with one drug remained the common therapy during this time. In 1996, the introduction of protease inhibitors along with a greater understanding of the HIV life-cycle led to the development of combination therapies involving three or more drugs – commonly referenced by the acronym HAART (highly active antiretroviral therapy). Regimens were also simplified as two or more drugs were combined into single pills. Both advancements were shown to improve therapy adherence and overall effectiveness at suppressing HIV viral load.[13,14] Mortality, transmission and CD4 recovery endpoints were also improved by beginning HAART treatment at earlier stages of the HIV infection.[15-18] Further, HAART therapy as pre-exposure prophylaxis also appeared effective at reducing transmission of HIV.[19-21] Ultimately, HIV-infected individuals with proper sustained HAART therapy could significantly increase

their number of years of life-expectancy and remain asymptomatic.[22-24] Among those diagnosed early in their HIV infection, life-expectancies achieved with HAART therapy were similar to that of their HIV-naïve counterparts.[25] As such, current CDC guidelines recommend initiation of HAART therapy for all individuals with HIV infection regardless of CD4+ count.[26] As pre-exposure prophylaxis (PreP), HAART therapy is also recommended as a method to reduce risk of HIV-infection acquisition amongst at-risk individuals.[27]

1.3 HIV Burden and Detection

Despite the advancements in HIV medications, the majority of people living with HIV (PLHIV) are not regularly receiving treatment with antiretroviral therapy (ART). Of the 1.2 million estimated PLHIV in the United States, almost 14% are unaware of their infection. Only 37% of the PLHIV in the United States were prescribed ART with 30% of PLHIV being virally suppressed within a year of HIV diagnosis.[28] In recent years, there were still over 15,000 new AIDS cases and over 16,000 AIDS-related deaths annually in the United States alone.[7] Among PLHIV, those who were not virally suppressed were up to 94% more likely to transmit the infection to another.[29] Each individual newly-infected with HIV is estimated to cost approximately $380,000 for lifetime treatment.[30] Although this treatment is cost-effective from an individual standpoint, overall cost burden still increases with each incident HIV case. Given the large proportion of PLHIV not receiving ART, there is much room for improvement in the number of adverse health events and HIV-related costs that can be achieved from more comprehensive treatment coverage.

A major part of expanding treatment coverage is the detection of HIV-infected persons who are unaware of their infection. Testing tools for HIV infection have improved over the years with regards to ease of use, rapid results, and diagnostic abilities. Current laboratory-based

serology tests are now individually capable of detecting and reporting results for HIV-1 Antibody (Ab), HIV-2 Ab, and p24 antigen (Ag). Window periods for these tests have also become shorter as the test sensitivity for infections in early stages increases.[31] The use of finger-stick blood-based or oral fluid-based rapid tests, which provide more immediate diagnoses, have become more widespread, with home testing kits available as well. Another option, nucleic acid-based tests, can provide even earlier detection of HIV infections than Ab tests.[32] Different testing algorithms involving one or more of the available tests also allow for detection of acute HIV infections, and can provide equivalent (or better) alternatives to traditional Western Blot (WB) for HIV diagnosis confirmation.[33,34] The HIV diagnostic test advancements together with current CDC screening guidelines that recommend opt-out screening of patients in all healthcare settings could potentially increase the detection rate of new HIV cases. It is important then that treatment coverage of HIV+ individuals not lag behind in pace to the detection of newly-infected persons. Addressing and reducing current gaps in treatment may require more understanding of factors related to whether or not an individual ultimately receives HIV care and treatment.

1.4 HIV Care Continuum Model

Maintaining consistent engagement in care is important for effective treatment and viral suppression of HIV.[35] The CDC uses the HIV care continuum to monitor steps between identification of HIV infection and viral suppression.[36] The HIV care continuum tracks the proportion of people with HIV in the following progression of steps: 1) diagnosed with HIV infection; 2) linked to care; 3) engaged or retained in care; 4) prescribed antiretroviral therapy; and 5) virally suppressed. The denominator used for these proportions defines the approach of the continuum, either prevalence-based or diagnosis-based. A prevalence-based HIV care continuum defines the denominator as the total number of PLHIV. The other approach, the

diagnosis-based HIV care continuum specifies the denominator as the number of PLHIV who have been diagnosed. By definition then, the first step of the continuum (proportion diagnosed with HIV infection) for the diagnosis-based approach equals one and is usually not graphically displayed. The prevalence-based continuum is generally applied to broader populations since the denominator of all PLHIV must be estimated from statistical modeling. In situations for which the total number of PLHIV is difficult to estimate such as sub-populations based on race and sexual orientation or undefined catchment areas, the diagnosis-based approach is more applicable.

The following descriptions are of the numerators for each step of the HIV care continuum as defined by the CDC. The first step, diagnosed with HIV infection, represents the number of people currently diagnosed and living with a HIV infection. Linked to care estimates the number of diagnosed PLHIV with at least one documented viral load or CD4+ count within 3 months of diagnosis during a one year period. Engaged/retained in care is defined as diagnosed PLHIV with at least two documented viral loads or CD4+ counts three months apart within a one year period. At least one documented prescription for ART within the observation year constitutes "prescribed ART". The final step, viral suppression, shows the number of diagnosed PLHIV with their most recent documented HIV viral load in the observed year being below 200 copies/mL.[36]

1.5 Knowledge, Difficulties, and Future Steps based on HIV Care Continuum

The HIV care continuum model is widely used by public health and research entities, but the definitions of each step within the model may differ across usage.[37] Amongst the steps of the model, the definitions for linkage and retention tend to vary the most. The general intent of the terms seems constant – that is, linkage and retention are attempting to characterize the situations

in which an HIV-infected individual initiates care, and then consistently maintains that care (ie. process of care).[38] However, there is no accepted gold-standard approach to defining linkage and retention. Definitions for both these terms may involve clinic visits, CD4+ count/viral load tests, or both, as well as a time factor. Regardless of the exact definition incorporated, linkage and retention are often shown to be positively associated with HIV viral suppression. Indeed, the initiation of care, either indicated by a clinic visit or laboratory test(s), within specified time periods increases probability of HIV viral suppression.[39] A dose-response relationship has also been shown between time to linkage after a HIV diagnosis and proportion of those virally suppressed after one and two years.[40] Likewise, more consistent adherence to clinic visits (ie. retention) was also related to more desirable HIV viral load endpoints.[41-44] Further, continued engagement with care after HIV viral suppression decreased the probability of viral rebound.[45] These associations between retention and viral suppression may be even more pronounced among those highly immunocompromised.[46] Despite the evidence showing the importance of linkage and retention in achieving HIV viral suppression, retention in care of people diagnosed with HIV is still only 46% in the United States.[47] Even in situations with little or no financial barriers, retention remains low.[48] As such, a central vision of the National HIV/AIDS Strategy is to improve identification of HIV infected persons and increase their access to ART.[49]

Multiple studies have examined factors related to linkage and retention outcomes. Associations have been commonly seen with demographics such as age, race/ethnicity, sexual orientation and drug use. Younger age groups[50-52] and illicit drug users[50,53,54] are consistently shown to be related to poorer linkage or retention measures. Both direct and inverse associations with linkage/retention measures have been observed for the sexual orientation of men who have sex with men (MSM).[51,55] Black or non-white ethnicities have also been associated with poorer

linkage/retention outcomes.[50,54,55] However, studies based on uninsured populations have found no difference in linkage or retention by race/ethnicity, suggesting possible confounding by socioeconomic status.[52,53] The immune health of the HIV patient may also have a role in linkage and retention. Persons with lower CD4+ counts at diagnosis were more consistently engaged in care than those with higher CD4+ counts.[52,53] Although some factors are consistently associated with linkage and retention measures across studies, the same consistency for many other demographic and behavioral characters have not been observed. The absence of a gold-standard definition for linkage and retention may contribute to inconsistent findings between studies. Further, a lack of observed associations for other factors may also be dependent on the specified endpoints, in that the linkage or retention definition used may not best portray engagement in care for that population. If the ultimate goal of engagement in care is eventual HIV viral suppression, then perhaps the quality of a linkage or retention definition should be based on its ability to predict viral suppression. Given the variations between populations, a single universal definition for linkage and retention that is the most germane choice across populations may not exist. Thus, in this regard, an important step may be to also examine the appropriateness of the linkage and retention definitions for any given population of interest. Better understanding of the proper measures for linkage and retention and the associated factors may more effectively guide strategies to improve overall viral suppression.

Most of the current research on factors associated with the HIV care continuum has focused on single steps in the continuum as the endpoint. As noted above, previous studies have examined predictors of linkage or retention. Other studies have delved into potential associations with being prescribed ART or achieving viral suppression.[56-58] But the underlying denominators in these studies have been a single static population: either those who were

diagnosed with HIV or those PLHIV who have initiated care. Few studies to date have followed a cohort of PLHIV through the entire progression of steps in the care continuum and examined factors associated with moving forward to each subsequent step. Focusing on only a single endpoint in the continuum such as viral suppression among those diagnosed with HIV is akin to a metaphorical black box approach. If the HIV care continuum serves as the framework to monitor progress towards viral suppression, then examining the model in its entirety would be more advantageous than focusing on single aspects. For example, if certain factors among those diagnosed with HIV have been observed to be associated with eventual viral suppression, a natural follow-up query would be to know if these relationships remain significant in between each adjacent step as well. This analytic approach would refine our understanding of the care continuum to a greater level of detail and in turn, may help direct more targeted policies towards improving overall HIV service delivery.

A major difficulty in producing HIV care continuums and corresponding analyses is the aggregation of the necessary data. Information on new diagnoses, physician/clinic visits, prescription information and ongoing laboratory test results are all necessary. Most often, this information will not be available through a single source, but must be gathered from different agencies by the researcher or some other entity. Further, once the information is collected, the different parts must then be compiled and matched together by each patient. The final working data and the process of reaching that point , especially when extracting from surveillance data, present a host of challenges including issues related to consolidation of data from sources with differing data quality and completeness, biases of estimates based on proxy measures, and validity concerns due to migration of the population.[56] Due to the complexity and limitations of the data required, many HIV care continuums are based on either public health surveillance data,

records from single clinic or clinics within the same region, or separately-funded study cohorts. Surveillance-based HIV care continuums usually present only broad population estimates without the ability to provide more stratum-specific estimates. Further, with surveillance data, proxy measures must often be used in lieu of actual clinic visit records.[56] On the other hand, continuum estimates based on information from clinics may allow for more specific analyses, better linking of data, and use of actual clinic visit data instead of proxies. However, clinic data-based continuums may be more geographically limited and subject to the same migration-related validity issues as the surveillance-based estimates. Recruiting more clinics to broaden the representation area would then require additional human and financial resources. A third option, study cohort data, may allow for more specific analyses and estimates, but require higher costs to maintain. An ideal source of data for generating a HIV care continuum would be a centralized system serving multi-region sites that routinely documents all the necessary information, can follow patients over time, and does not require additional resources aside from the original intended operating costs. Such a centralized system would be less susceptible to many validity issues related to population surveillance-based continuums.[56] A real-world example similar to this hypothetical ideal system is that of AIDS Healthcare Foundation (AHF), an AIDS service organization that operates as a HIV-screening and HIV-care provider across multiple jurisdictions in the United States with a unified HIV screening, administrative, and medical records system.

1.6 AIDS Healthcare Foundation

AIDS Healthcare Foundation (AHF) is a non-profit global organization that provides comprehensive HIV medical care, specialists, medications, and counseling services. Based in Los Angeles, AHF provides its services in 15 states domestically regardless of clients' ability to

pay. AHF is currently the largest AIDS service organization in the world and maintains a strong community presence through its medical, advocacy, and research programs, and collaborations with public and other private entities. They also implement specific activities targeted towards high-risk populations such as MSM, women, minorities, and other more vulnerable groups. The client population at AHF is predominantly men but is diverse with regards to race/ethnicity and age. One reason for this diversity is the wide HIV detection effort utilized by AHF. Both active and passive approaches to HIV testing are employed by AHF. Active surveillance for HIV involves mobile testing units that can deploy to different areas of the community and provide rapid HIV testing. General testing for HIV occurs at AHF Men's Wellness Centers, other AHF fixed-sites (eg. Out of the Closet thrift stores), and AHF-partnered community clinics. The diversification of testing options and the geographic spread of the numerous testing sites allow AHF to reach more segments of the community than that of traditional single-site clinics. Further, the availability of in-person HIV counseling services by AHF may also provide incentive for individuals to choose an AHF location as their HIV testing site.[57] Clients newly detected with HIV at AHF sites generally stay within the AHF system – those detected at partnered-sites are also referred to AHF for all aspects of HIV care.

Client information on administrative billing, appointments, laboratory test results, prescriptions and wellness for all AHF regions can be accessed centrally. Many clients have an ongoing relationship with AHF with regular visits for general wellness or other sexual health concerns regardless of HIV status. In fact, a large proportion of the clients accessing AHF services are not infected with HIV. Clients report high satisfaction with AHF with overall ratings in the high 90 percent range in recent years. These high client satisfaction ratings likely translate to high client loyalty towards AHF.[58] As such, it is reasonable to assume that clients

who migrate will likely stay within the AHF provider network if an AHF site is still local and accessible. Thus, given the multitude of AHF and affiliated sites nationwide, the high client satisfaction ratings, and minimal financial barriers to access AHF services, the AHF system may be more adept at following a client after a migration than compared to single site clinics or public sector surveillance systems. In addition, the high client loyalty may lead to improved retention within the AHF system enabling the monitoring of a client's HIV health and treatment status for more extended periods of time. From a healthcare delivery perspective, the basis of the high client loyalty may result in more desirable health outcomes.[59] From a research perspective, the lengthy follow-up times due to client loyalty provide the opportunity to examine long-term endpoints. With the combination of relevant information and the quality and length of follow-up, the AHF data system is an optimal source for applying and evaluating multiple aspects of the HIV care continuum.

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CHAPTER 2

Factors associated with Progression towards HIV Viral Suppression among the Framework of the HIV Care Continuum

2.1 ABSTRACT

Background: Suppression of viral load to near undetectable levels is the goal of HIV care. The HIV Care continuum is a framework of stages to monitor progression towards this goal. Previous studies on associated factors have focused on single stages within the continuum. A comprehensive analysis of the entire care continuum based on a single population would refine our understanding.

Methods: Relevant information was extracted for clients diagnosed with HIV and referred to care at AIDS Healthcare Foundation (AHF) between January 1, 2012 and December 31, 2013. The following CDC-defined care continuum measures were derived for each client: linkage to care, retention in care, antiretroviral therapy (ART), and one-year viral suppression (VS) using both dependent and independent methodology. The HIV care continuum was estimated for the client population. Associations with demographic and structural factors at each stage of the continuum were evaluated with logistic regression.

Results: A total of 3,229 clients were included in the analyses. The estimates of the HIV care continuum stages were: 78.5% linked; 56.2% retained; 53.3% ART; 36.1% VS (dependent methodology); and 78.5% linked; 57.4% retained; 73.5% ART; 40.5% VS (independent methodology). The demographic factors, age, black ethnicity, and homeless were associated

with VS among all clients. Age and homeless were also associated with progressing to each continuum stage. Other covariates, CD4 (baseline), ethnicity, and time to linkage were significantly associated only with certain stages.

Conclusion: Several factors including age, race/ethnicity, homelessness, and CD4 count showed consistent patterns of associations in the continuum. Results demonstrate the specific nature of associations with regards to timing within the continuum. Overall associations with viral suppression may not persist at every stage of the continuum. Evaluations should be specific enough to identify the period or stage at which covariates of interest are of most influence.

Keywords: HIV Care Continuum; viral suppression; linkage; retention; ART

2.2 INTRODUCTION

The overall quality of life for individuals with HIV is dependent on suppression of the HIV virus. Suppressing viral load to near undetectable levels may increase life-expectancy to that comparable with HIV-naïve persons[1,2], prevent onset of HIV-related symptoms[3,4], and reduce further transmission of HIV.[5-8] Initiation and consistent engagement in care after diagnosis of HIV establishes the foundation for achieving viral suppression along with associated improved long-term health outcomes.[9] The HIV care continuum model characterizes the process of achieving this end goal with the following progression of measurable steps: 1) HIV diagnosis, 2) linkage to care, 3) retention in care, 4) antiretroviral therapy (ART) prescription, and 5) viral suppression.[10] Even with variations in the precise definitions of the linkage and retention measures[11], reaching either of these stages is consistently associated with eventual viral suppression.[13-17] Thus, it is important during the clinical management of persons with HIV to ensure that the intermediate stages of the HIV care continuum are achieved. Current national estimates of the HIV care continuum for the estimated 1.03 million persons known to be living with HIV in the United States are: 46% linked and retained in medical care; 43% prescribed ART; and 35% virally suppressed.[17]

Linkage and retention outcomes have been shown to be associated with demographics such as age, race/ethnicity, sexual orientation and drug use. Younger age groups[18-20] and illicit drug users[18,21,22] are consistently shown to be related to poorer linkage or retention measures. Both direct and inverse associations with linkage/retention measures have been observed for the sexual orientation of men who have sex with men (MSM).[19,23] Black or non-white ethnicities have also been associated with poorer linkage/retention outcomes.[18,22,23] However, studies based on uninsured populations have found no difference in linkage or retention by race/ethnicity,

suggesting possible confounding by socioeconomic status.[20,21] The immune health of the HIV patient may also have a role in linkage and retention. Persons with lower CD4+ counts at diagnosis were more consistently engaged in care than those with higher CD4+ counts.[20,21] Other studies have also examined predictors of viral suppression among persons diagnosed with HIV.[24-26]

An approach focusing on multiple endpoints specific to the HIV care continuum using a single study population may refine our understanding of the care continuum to a greater level of detail. AIDS Healthcare Foundation (AHF) is a non-profit global organization that provides comprehensive HIV medical care, specialists, medications, and counseling services regardless of clients' ability to pay. AHF uses a unified administrative and medical records system for all of its HIV screening and medical care services across multiple jurisdictions. With the central longitudinal data system from AHF, we sought to examine the consistency of predictors throughout the progression of HIV care continuum stages. This type of analysis may help interventions more effectively target people specific to their HIV care continuum stage to ensure continued progression towards viral suppression. For example, if a known predictor of viral suppression is no longer significant conditional on achieving an intermediate stage of the continuum, then interventions focusing on that factor may not be as effective for persons in that continuum stage and vice-versa.

2.3 METHODS

Study Population

For this study, we included all clients diagnosed with a HIV infection and referred to AHF for linkage and care between January 1, 2012 and December 31, 2013. This population

included clients who were diagnosed at an AHF-affiliated facility or a partner-site at any of the multiple regions served including California, District of Columbia, Florida, Georgia, Michigan, Nevada, North Carolina, New York, Ohio, Pennsylvania, and Texas. The start date of January 1, 2012 was chosen to correspond with change in AHF central staff related to the data management of relevant information, so as to have the most complete data. December 31, 2013 was set as the end date to allow for at least a year of viral load (VL) measurements post-diagnosis. Clients with a missing date of HIV diagnosis were excluded. For analyses involving viral suppression, clients with no available VL reported within the time frame of interest were also excluded. Because information regarding sexual orientation was missing for over half of the clients, we did not include MSM (men who have sex with men) status as a variable in the analysis. However, over 90% of male clients with available sexual orientation data were MSM.

HIV Care Continuum Measures

All relevant information regarding diagnoses, clinic intake, prescriptions, and laboratory results were extracted from AHF data systems. The overall proportion of clients having reached each HIV care continuum stage was estimated, and a dichotomous (yes/no) variable for having reached each stage was also generated. All clients diagnosed with HIV and referred to AHF for care was used as the denominator for each of the overall continuum measurements. Each step of the HIV care continuum was based on definitions by the Center for Disease Control and Prevention (CDC) and operationalized as study outcomes as follows.[10]

- Linked to care: laboratory record of at least one viral load or CD4+ test within 90 days of the HIV diagnosis date
- Retained in care: laboratory record of two or more viral load or CD4+ test with at least two of the tests separated by 90 days within one year after the HIV diagnosis date

- Prescribed ART: record of at least one ART prescription within 90 days of HIV diagnosis
- Viral Suppression: documented VL measurement closest in date to one year following HIV diagnosis being ≤ 200 copies/mL; in order to broaden the range of available VL measurements, this definition was expanded to include VL tests up to 120 days past the one-year date[14]

Predictors

Individual and structural level factors were dichotomized into the following covariates: male gender (at birth), age over 35, Black (non-Hispanic), Hispanic, other ethnicity, homeless, low CD4 count (< 200 copies/μL), time to linkage (within 30 days of HIV diagnosis), Partner-site of diagnosis, California site of diagnosis, and winter season diagnosis. All covariate measurements were at baseline, except for time to linkage which is only applicable to clients that are linked to care. Male gender at birth includes all men and male-to-female transgendered versus all women and female-to-male transgendered. Low CD4 count is based on the CD4 measurement nearest and within 90 days of the date of diagnosis. Time to linkage shows if a linked client was linked to care within 30 days of HIV diagnosis or referral. Partner site indicates that the client was diagnosed at a site not affiliated with AHF and then referred to AHF for care. California site refers to the client being diagnosed at a site located in the state of California. Winter season indicates that the client was diagnosed during the winter months of December through March. Covariate categories were based on previous definitions in literature or sensible groupings.

Study Analyses

The overall HIV care continuum was estimated for the eligible study population with both dependent and independent methodologies. The dependent methodology requires individuals to have achieved the previous stage in order to be included in estimates for any given stage, whereas no such condition is required for the independent methodology.[27] Consistent with previous literature, performance through the care continuum was underestimated with the dependent methodology. Further multivariate analyses were conducted with groupings based on the independent methodology. To assess the consistency of predictors of viral suppression throughout the HIV care continuum, the following probabilities were modeled with multivariate logistic regression: 1) viral suppression among all diagnosed; 2) linkage among all diagnosed; 3) retention among all linked; 4) ART prescription among all retained; 5) viral suppression among all retained; and 6) viral suppression among all with ART prescription. For stratified analyses, all predictors were included in every model with the exception of low CD4 and time to linkage. Since the presence of a CD4 measurement within 90 days of diagnosis coincides with the definition of linkage, low CD4 was not included as a covariate in the models based on all persons diagnosed (models 1 and 2). Time to linkage was included only in models based on clients already linked to care (models 3, 4, 5, and 6). For univariate analyses, chi-square p-values are reported. Missing data were excluded from analyses. All analyses were performed with SAS *v*9.4 (SAS Institute, Cary, North Carolina, USA).

2.4 RESULTS

Baseline Characteristics

A total of 3,229 clients were identified as diagnosed with HIV and referred to AHF for care during the study period, with an increase from 1,167 in 2012 to 2,062 in 2013 (Table 2-1).

Clients diagnosed in both years were similar with regards to baseline demographics. Both 2012 and 2013 clients were predominantly male at birth (91.9% and 87.0%) with approximately half over 35 (48.7% and 51.1%) as well as mean age over 35 (36.3 and 37.2). Nearly three quarters of the clients were minorities in both years (70.5% and 74.8%). The proportion with CD4 < 200 copies/μL was low and similar for each year (15.6% and 17.4%). Being homeless was also rare in both years (4.6% and 3.5%). Relatively more clients were diagnosed in California in 2012 (68.3%) than in 2013 (40.4%). Despite the difference in region of diagnosis between the two years, the proportion of clients diagnosed from partner sites (61.4% and 59.2%) and during the winter months remained similar by year (28.6% and 30.1%).

HIV Care Continuum

The HIV Care continuum for both the dependent and independent methods is represented in Figure 2-1 and Figure 2-2 respectively. By definition, the linkage measures were the same in both methodologies. Other than linkage, performance estimates for the continuum steps were higher in the independent methodology than in the dependent methodology. In both methodologies, linkage in 2012 (79.3%) was higher than that in 2013 (77.9%). However, in both methodologies, performance for continuum steps after linkage was better in 2013 than in 2012. For the dependent methodology, the continuum estimates for the 3,769 clients diagnosed in the two years were: 1) 78.5% linked; 2) 56.2% retained; 3) 53.3% prescribed ART; and 4) 36.1% virally suppressed at one year. The corresponding estimates under the independent methodology were: 1) 78.5% diagnosed; 2) 57.4% retained; 3) 73.5% prescribed ART; and 4) 40.5% virally suppressed.

Multivariate Analyses

In multivariate analyses, viral suppression among all diagnosed clients was directly associated with age over 35 and year of diagnosis (2013), and inversely associated with Black ethnicity and homelessness (Table 2-2). The most consistent significant associations throughout the continuum stages were observed for age over 35, homelessness, and CD4 < 200 copies/μL (low CD4). Age over 35 was a significant positive predictor in every one of the multivariate models. Homelessness was also consistently associated (inversely) with the outcome in all models except for ART prescription among all retained clients. The covariate low CD4 was not included in models 1 and 2 (those involving all client diagnosed), but was a significant predictor in each of the other models. Low CD4 was positively associated with retention among all linked clients (Adjusted odds ratio (AOR)=1.32, 95% Confidence Interval (CI)=1.03, 1.70) and ART prescription among all retained clients (AOR=2.69, 95%CI=1.15, 6.25). However, the association with low CD4 became negative for viral suppression among all retained clients (AOR=0.72, 95%CI=0.55, 0.95) and viral suppression among all clients prescribed ART (AOR=0.52, 95%CI=0.41, 0.66). (Tables 2-3, 2-4)

Significant associations observed with other covariates were less consistent. (Tables 2-4) Black (non-Hispanic) ethnicity was a significant predictor only when viral suppression was the outcome: viral suppression among retained clients (AOR=0.60, 95%CI=0.45, 0.80) and clients prescribed ART (AOR=0.70, 95%CI=0.55, 0.90). Similarly, for year of diagnosis (2013), significant associations were also only observed with viral suppression – among retained clients (AOR=1.57, 95%CI=1.24, 1.97) and among those prescribed ART (AOR=1.50, 95%CI=1.23, 1.84). Partner site was positively associated only with linkage among all diagnosed clients (AOR=2.39, 95%CI=1.99, 2.88) and ART prescription among all retained clients (AOR=1.68, 95%CI=1.07, 2.63). Site location in California was only predictive of linkage (AOR=1.98,

95%CI=1.62, 2.44) and of retention (AOR=1.36, 95%CI=1.12, 1.67). Time to linkage was only associated with retention among linked clients (AOR=1.40, 95%CI=1.04, 1.87). Despite possible differences in clinic attendance by season[28], diagnosis during the winter months was not predictive of any outcome.

2.5 DISCUSSION

Previous studies regarding the HIV care continuum have frequently focused on only single endpoints within the continuum. As such, gauging the impact of predictors throughout the course of the continuum often requires piecing together results with limited comparability due to the different populations and methods upon which they were based.[29] The potentially fluid nature of these associations should ideally be examined in a consistent population as it progresses through the continuum. Following the same or similar population over time and continuum stages as we did in this current analysis provides a more systematic approach to understanding the continuum as a whole. Further, our use of person-year in determining continuum stages is preferable to the calendar-year methods in continuums based on surveillance data.

The HIV care continuum for this population was generated using both the dependent methodology, which requires individuals to have achieved prior stages in order to be counted at any stage, and the independent methodology which does not require this condition.[27] By definition, the proportions for each stage of the continuum after linkage were higher using the independent methodology. From an analytic perspective, the difference in the measurements between the two methodologies suggests that among the intermediate steps (as defined here), a given stage is not necessarily a requisite of a subsequent stage. Since the definition of retention

is closely related to the linkage definition in our analysis, the retention measures are understandably similar between the two methodologies. However, the >20% higher estimate of ART prescription from the independent methodology highlights the distinct nature of the stages and suggests that there may not be a set temporal order between retention and ART. As such, our multivariate analyses reflected this distinction with a separate model for viral suppression among those retained and for viral suppression among those prescribed ART. Although the intermediate stages may not be necessary components for later stages, it is not to imply that there is no association between the stages. Our data indicate that the probability of achieving any given continuum stage after linkage is highest if the client has already reached the stage prior (not shown). These facets are the reasons we approached the care continuum as a progression of steps for the multivariate analyses, but employed populations for each analytic model based on the independent methodology.

The HIV care continuum values for AHF compare favorably to the national estimates.[17] Viral suppression at one year (52.5%) for AHF is higher than national estimates and consistent with the magnitude of the corresponding retention and ART prescription measures. The centralized aspect of the HIV care and counseling services at AHF and of the corresponding data may contribute to this higher observed performance. However, almost a quarter (22.5%) of those classified as virally suppressed did not have a VL measurement within 120 days of one-year post-diagnosis (±120 days; a 240 day span) and were thereby based on VL measurements from earlier in the year. And in total, almost half (46.4%) of the clients (virally suppressed or not) did not have a viral load measurement during this same window of time (±120 days of one-year post-diagnosis). Long term VL monitoring has been observed to improve ART adherence[30], which is crucial for sustained viral suppression.[31] Thus, additional attention should be directed

on addressing this gap in VL monitoring. Further, for 22.7% of clients classified as not virally suppressed, at least one suppressed VL measurement had been observed at an earlier point. This percentage (22.7%) is almost double the expected rate of viral rebound for those adhering to ART shown in a previous study.[32] As such, issues such as non-adherence and interruption in treatment are likely to be significant factors in the inability to maintain viral suppression in these clients. Despite the high overall measurement of viral suppression in this population, performance for this end goal may be improved even more by focusing on continued follow-up and sustained ART treatment and adherence.

The most consistent predictors through each stage of the continuum were older age (>35), homelessness, and low CD4 count. The persistent associations throughout the continuum observed for older age (positive) and homelessness (negative) are in accordance with previous studies. Older age groups have been observed to be a consistent predictor of each aspect of the care continuum.[19,33,34] Further, when age is evaluated as a mediator, the need for completion of earlier stages in order to achieve viral suppression was only evident among younger age groups.[34] With regards to homelessness, the strong observed associations with failure to progress at each continuum stage are not surprising. The transient nature of homelessness is related to general non-adherence to various aspects of care and therapy.[35,36] Our results further support the need to address housing instability as a part of case management.[37]

Although not shown, clients with a low CD4 count at baseline were less likely to achieve one-year viral suppression than clients known to have CD4 of at least 200 copies/μL at baseline (adjusted OR=0.69, 95%CI=0.51, 0.92). This pattern is reflected in previous studies that observed either no association or increased viral failure among patients with lower baseline CD4 levels.[38-41] In our study, initial access to care and therapy does not appear to be of issue, as

clients with low CD4 were more likely to be retained and to receive ART. Rather, this overall association with viral suppression seems to be driven by the strong negative associations in the latter stages of the continuum following both retention and prescription of ART. This lower probability of achieving viral suppression even after retention and ART prescription among clients with low CD4 does not appear to be due to loss-to-follow-up or non-adherence to ART. In fact, clients with low baseline CD4 were more likely to have a one-year VL measurement as compared to any other client. Although there was no information available on actual adherence in our cohort, previous literature suggests that there is not likely to be a difference in non-adherence by baseline CD4 count either.[42] Instead, an inherent difference in individual responsiveness to ART may be a factor as disproportionately more clients with low baseline CD4 were referred to AHF from a partner site than were diagnosed directly at an AHF site. Our results may also reflect previous findings that patients starting therapy with lower CD4 levels have increased risk of AIDS progression and death.[43]

The overall association of Black (non-Hispanic) ethnicity with decreased viral suppression stemmed from the same association among clients already retained or prescribed ART. No difference was observed in the initiation and engagement of care (ie. linkage and retention) for Black (non-Hispanic) clients compared to White clients. Although lower retention in care among Black patients has been previously observed elsewhere,[18,22,23,44] this disparity was less consistent in studies based on clinics serving low-income populations.[20,21] As such, the lack of association with linkage and retention in this analysis was not surprising given that AHF provides services irrespective of one's ability to pay. However, the failure to achieve documented viral suppression after retention and ART prescription is concerning. Issues related to both loss-to-follow-up and adherence may contribute to the lower observed viral suppression.

First, Black (non-Hispanic) clients were less likely to have a VL measurement at one year (±120 days), which can serve as a proxy for lack of engagement with the AHF system. Prior literature has already suggested that differences in retention between ethnicities become more pronounced over the long-term.[45] It is possible then that factors specific to ethnicity influencing one-year viral suppression were not as relevant during the earlier portion of the year, the time period which our measures for linkage and retention primarily cover. For example, the humanitarian nature of AHF may remove the direct financial barrier of obtaining services, but cannot compensate for structural barriers on the client end. These barriers such as access to transportation, competing schedules, unstable housing, etc. may differ by ethnicity and hinder sustained engagement with care.[34] Another factor relevant to decreased viral suppression may be a possible lower adherence to ART among Black clients[46-48] and the corresponding effect on viral failure.[49] Further consideration directed towards adherence to care after initial retention and ART prescription is needed to address the ethnic disparity in viral suppression.

Initiation or linkage to care within 30 or 90 days has been shown to be associated with both higher proportion of viral suppression at a given time and faster time to viral suppression.[50-52] In our multivariate models, time to linkage (within 30 days) is a significant predictor only for retention among all linked clients. Interestingly, however, time to linkage is not associated with overall one-year viral suppression among linked clients in our data when adjusting for retention (not shown). Since linkage is positively associated with viral suppression (not shown), it appears that any initiation to care within 90 days (our definition for linkage) is the more important determinant of viral suppression in our data than the timing within the 90 days. Instead, the benefit of earlier linkage (within 30 days) is observed in the higher proportion of retention achieved. Once a client is retained, the timing of the initial linkage no longer appears to

influence eventual viral suppression. From a pure data perspective, early linkage within 30 days alone without further retention does not appear to be enough to improve viral suppression. This is not to counter the well-established biological benefits of starting ART treatment as early as possible. However, with regards to the continuum measures and program planning, ensuring continued engagement after initial linkage (whether early or late), is the more critical determinant of eventual viral suppression.

Several limitations must be considered when interpreting these results. As with all observational studies, causation cannot be definitively established. The potential for residual confounding remains as we did not have adequate information on certain demographics such as those related to social economic status, sexual orientation, and high-risk behaviors. Our study population may also not be generalizable to the overall population of new HIV cases surrounding the sites of diagnosis. The clientele at AHF are predominantly male with a high proportion of MSM, both of which exceed the proportions in new HIV infections nationally.[53] Some clients were also regular wellness clients prior to HIV diagnosis and may exhibit healthier behaviors than the general population. In addition, since clients were also referred from external sites, a portion of the clients new to AHF may not necessarily be newly-diagnosed with HIV. Behavior of persons newly aware of their HIV infection may differ from that of persons who already know their HIV status and/or have been previously engaged in care elsewhere. In both instances, these clients may undergo a different dynamic towards viral suppression than their counterparts.

Misclassification of viral suppression outcome due to use of VL measurement dates occurring in the entire year following diagnosis was also possible. As noted earlier, the outcome for a portion of clients were based on VL tests occurring within the first eight months after diagnosis. If viral status had changed closer to the one-year date, then a viral suppression

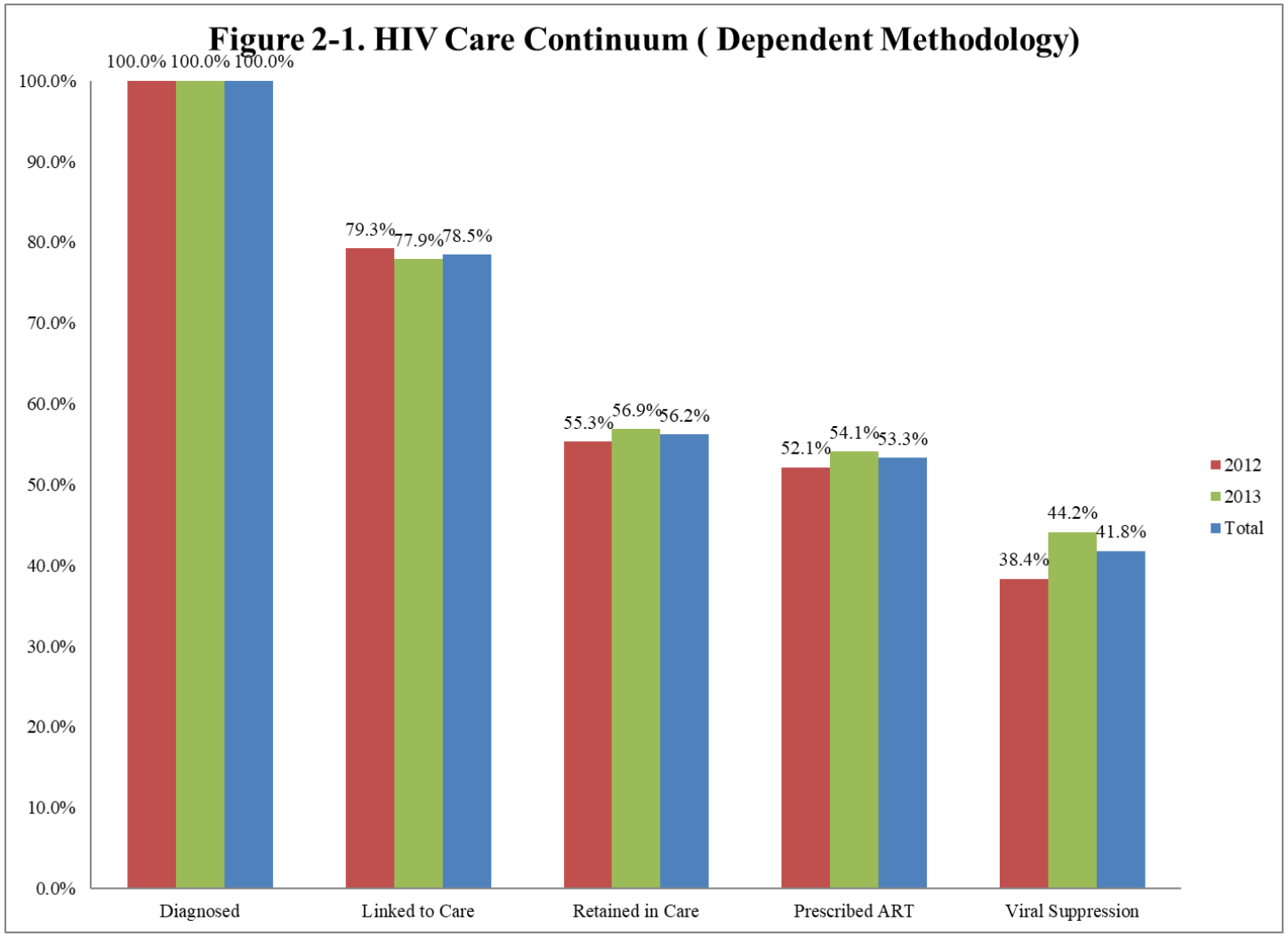
outcome based on earlier VL measurements would be inaccurate. Similarly, individuals who are lost to migration are also not reflected in the results. As with most studies involving HIV care continuums, this study lacked information on whether these clients continued to progress along the continuum stages elsewhere. If the overall continuum values for individuals similar to AHF clients were of interest, the continuum measures presented in this study would likely be underestimates of the truth. However, if the goal is to evaluate AHF-specific performance, then the continuum estimates would be valid representations of performance despite the loss-to-follow-up.

HIV care continuum measures consistent with those defined by CDC and other studies provided more external comparability for this study. However, the process of transitioning from HIV diagnosis to viral suppression is longitudinal and fluid in nature. Cross-sectional measures as we have used here may not be the best indicators for characterizing the whole scenario. For example, a cross-sectional single measurement of viral load may not allow differentiation between a viral blip and true viral failure.[54] Instead, longer-term longitudinal counterparts may be more proficient and accurate at capturing the true states of care engagement and viral suppression.[45] Further, linkage and retention measurements that incorporate additional appointment and visit information, even if still cross-sectional, may also provide more fidelity.[55] Despite some shortcomings, the definitions we used minimized the amount of missing values for outcome variables. This aspect was especially important given the depth of the multivariate analyses in this study. Given more extensive data, future analyses can build upon these results by using more comprehensive definitions for the continuum stages.

Conclusion

Following the same population throughout the HIV care continuum has provided further insight into: 1) identifying predictors along each stage of the continuum and of overall viral suppression; and 2) the dynamics of associations by allowing more standardized comparisons between continuum stages. As expected from previous literature, several factors including age, race/ethnicity, homelessness, and CD4 count showed consistent patterns of associations in the continuum. Differences due to other structural factors specific to HIV diagnosis including State of diagnosis site, year of diagnosis, and diagnosis site type were occasionally present but less consistently observed. These results demonstrate the specific nature of associations with regards to timing within the continuum. As shown in these analyses, an association between a covariate and viral suppression among all diagnosed may not persist at every stage of the continuum. The majority of associations in this study were observed in the latter portion of the continuum after retention and ART prescription. This pattern suggests that many of the forces determining viral suppression with regards to our covariates were active in the later periods that were less represented by our measures of linkage and retention. As such, expanded definitions of retention (eg. longitudinal measures) that can more fully capture these time periods may be necessary to better assess engagement in care and determine profiles for intervention. Further, future evaluations of factors affecting viral suppression should be specific enough to identify the period or stage at which the covariates of interest are of most influence. Consideration of the aforementioned issues may improve our comprehension of the social mechanism involved in viral suppression and potentially lead to more efficacious interventions.

TABLES AND FIGURES



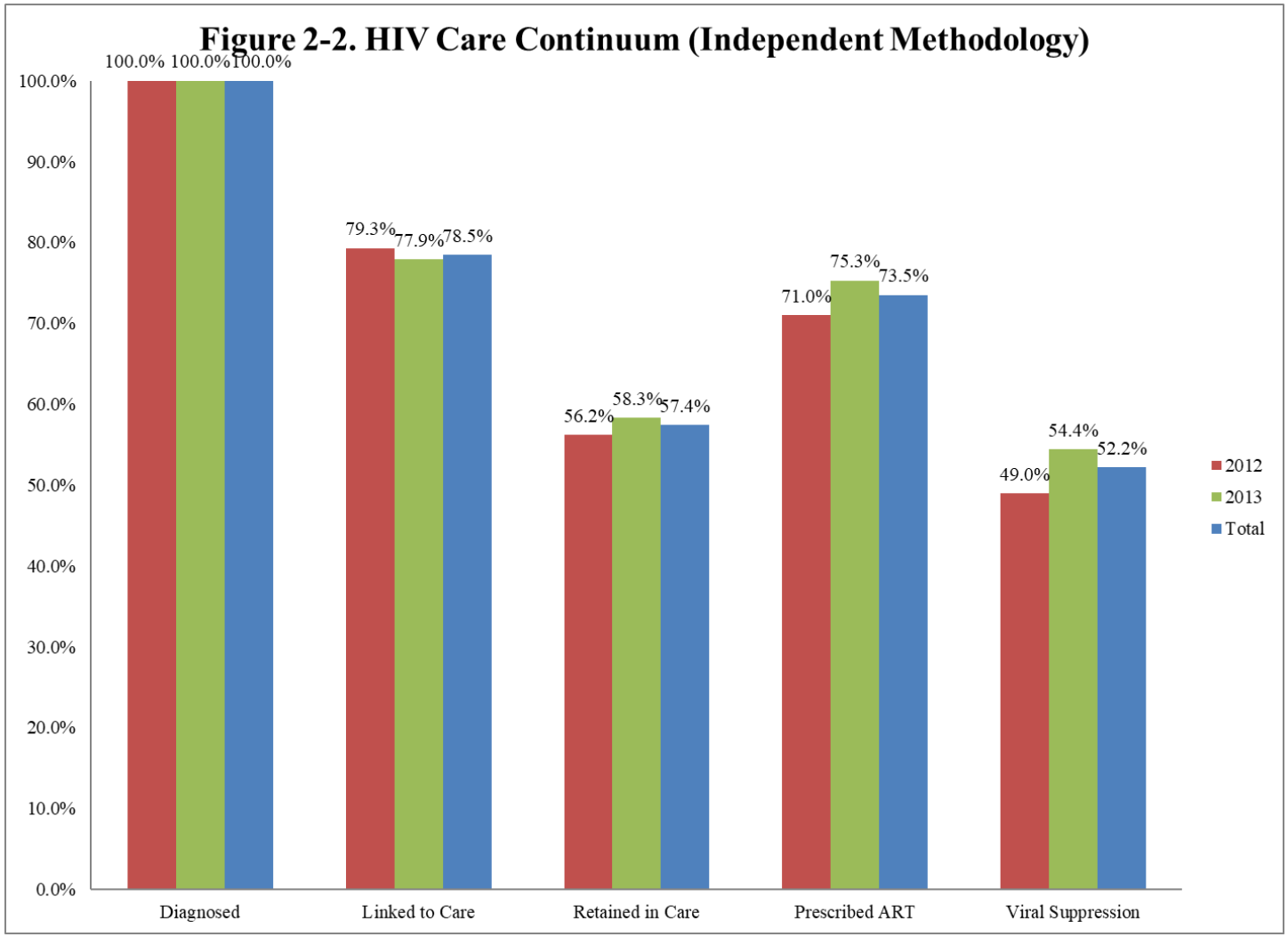


Figure 2-2. HIV Care Continuum (Independent Methodology)
100.0%
90.0%
80.0%
70.0%
60.0%
50.0%
40.0%
30.0%
20.0%
10.0%
0.0%
100.0% 100.0% 100.0%
79.3% 77.9% 78.5%
56.2% 58.3% 57.4%
71.0% 75.3% 73.5%
49.0% 54.4% 52.2%
Diagnosed
Linked to Care
Retained in Care
Prescribed ART
Viral Suppression
2012
2013
Total

Table 2-1. Baseline Characteristics by Calendar Year of HIV Diagnosis among HIV-positive clients at a national non-profit HIV care organization, 2012-2013

	2012	2013
Total	1167	2062
Male at birth	91.9	87.0
Mean age (standard dev.)	36.3 (11.4)	37.2 (11.5)
Age 35+	48.7	51.1
Race/ethnicity		
Black (non-Hispanic)	30.7	46.9
Hispanic	36.3	25.4
Other Ethnicity	3.5	2.5
White (non-Hispanic)	29.5	25.3
Homeless	4.6	3.5
CD4 count < 200 copies/μL	15.6	17.4
Linkage to care (w/in 30 days of diagnosis)	92.0	90.0
Site and Season of Diagnosis		
Outreach/Partner Site	61.4	59.2
California	68.3	40.4
Winter	28.6	30.1

Table 2-2. Multivariate analysis, Viral Suppression and Linkage among Diagnosed, HIV-positive clients at a national non-profit HIV care organization, 2012-2013

	Predictors of 1-year Viral Suppression among all diagnosed				Predictors of linkage among all diagnosed			
	VL1-year < 200 (n=1727)	VL1-year >200 (n=956)	Univariate *p* value	Multivariate odds ratio (95% CI)	Linked to care (n=2596)	Not linked to care (n=633)	Univariate *p* value	Multivariate odds ratio (95% CI)
Sex at birth								
Male	1542	857	0.77	0.93 (0.71, 1.22)	2313	552	0.18	0.98 (0.74, 1.30)
Female	185	99		1.00	283	81		1.00
Age at diagnosis								
35 and under	775	540		1.00	1265	343		1.00
35+	952	416	<0.0001	1.53 (1.29, 1.80)	1331	290	0.01	1.06 (0.88, 1.28)
Race/ethnicity								
Black (non-Hispanic)	634	436	<0.0001	0.66 (0.53, 0.82)	1022	302	<0.001	0.86 (0.68, 1.09)
Hispanic	540	270	0.10	0.97 (0.78, 1.20)	794	153	<0.01	1.14 (0.88, 1.46)
Other	51	20	0.18	1.23 (0.71, 2.13)	73	20	0.64	0.75 (0.44, 1.29)
White (non-Hispanic)	502	230	--	1.00	707	158	--	1.00
Homeless at diagnosis								
Yes	37	60	<0.0001	0.33 (0.22, 0.51)	93	34	0.04	0.50 (0.33, 0.76)
No	1690	896		1.00	2503	599		1.00
CD4 count at diagnosis								
<200	--	--	--	--	--	--	--	--
≥200	--	--	--	--	--	--	--	--
Time to linkage								
Within 30 days	--	--	--	--	--	--	--	--
After 30 days	--	--	--	--	--	--	--	--
Site of diagnosis								
Partner Site	1125	601	0.24	1.11 (0.93, 1.32)	1670	267	<0.0001	2.39 (1.99, 2.88)
AHF Site	602	355		1.00	926	366		1.00
Region of diagnosis								
California	923	504	0.72	1.01 (0.84, 1.21)	1406	223	<0.0001	1.98 (1.62, 2.44)
Other States	804	452		1.00	1190	410		1.00
Season of diagnosis								
Winter	494	301	0.12	0.84 (0.71, 1.01)	775	180	0.48	0.91 (0.75, 1.11)
Non-winter	1233	655		1.00	1821	453		1.00
Year of diagnosis								
2012	594	393		1.00	962	205		1.00
2013	1133	563	<0.001	1.40 (1.18, 1.67)	1634	428	0.03	1.01 (0.83, 1.24)

Table 2-3. Multivariate analysis, Retention among Linked and ART Prescription among Retained, HIV-positive clients at a national non-profit HIV care organization, 2012-2013

	Predictors of retention among all linked				Predictors of ART prescription among all retained			
	Retained in care (n=1869)	Not retained in care (n=691)	Univariate *p* value	Multivariate odds ratio (95% CI)	Prescribed ART (n=1779)	Not prescribed ART (n=90)	Univariate *p* value	Multivariate odds ratio (95% CI)
Sex at birth								
Male	1670	610	0.43	1.05 (0.79, 1.41)	1595	75	0.06	2.03 (1.10, 3.75)
Female	199	81		1.00	184	15		1.00
Age at diagnosis								
35 and under	874	373		1.00	816	58		1.00
35+	995	318	<0.01	1.28 (1.07, 1.54)	963	32	<0.001	1.86 (1.17, 2.96)
Race/ethnicity								
Black (non-Hispanic)	717	293	0.06	0.85 (0.67, 1.08)	681	36	0.74	0.96 (0.54, 1.70)
Hispanic	570	216	0.71	0.83 (0.65, 1.05)	541	29	0.72	1.01 (0.57, 1.78)
Other	52	17	0.66	0.92 (0.51, 1.65)	51	1	0.32	2.92 (0.38, 22.2)
White (non-Hispanic)	530	165	--	1.00	506	24	--	1.00
Homeless at diagnosis								
Yes	53	40	<0.001	0.44 (0.28, 0.67)	49	4	0.35	0.70 (0.24, 2.04)
No	1816	651		1.00	1730	86		1.00
CD4 count at diagnosis								
<200	332	95	0.02	1.32 (1.03, 1.70)	326	6	<0.01	2.69 (1.15, 6.25)
≥200	1537	596		1.00	1453	84		1.00
Time to linkage								
Within 30 days	1713	615	0.04	1.40 (1.04, 1.87)	1626	87	0.07	0.41 (0.13, 1.32)
After 30 days	156	76		1.00	153	3		1.00
Site of diagnosis								
Partner Site	1217	447	0.84	0.94 (0.78, 1.15)	1171	46	<0.01	1.68 (1.07, 2.63)
AHF Site	652	244		1.00	608	44		1.00
Region of diagnosis								
California	1040	347	0.01	1.36 (1.12, 1.67)	991	49	0.81	0.91 (0.56, 1.50)
Other States	829	344		1.00	788	41		1.00
Season of diagnosis								
Winter	556	205	0.97	0.98 (0.80, 1.19)	529	27	0.96	0.96 (0.60, 1.54)
Non-winter	1313	486		1.00	1250	63		1.00
Year of diagnosis								
2012	682	270		1.00	645	37		1.00
2013	1187	421	0.23	1.20 (0.99, 1.45)	1134	53	0.35	1.22 (0.77, 1.92)

Table 2-4. Multivariate analysis, Viral Suppression among Retained and Prescribed ART, HIV-positive clients at a national non-profit HIV care organization, 2012-2013

	Predictors of 1-year Viral Suppression among all retained				Predictors of 1-year Viral Suppression among all prescribed ART*			
	VL1-year < 200 (n=1411)	VL1-year >200 (n=458)	Univariate *p* value	Multivariate odds ratio (95% CI)	VL1-year < 200 (n=1586)	VL1-year >200 (n=662)	Univariate *p* value	Multivariate odds ratio (95% CI)
Sex at birth								
Male	1265	405	0.46	1.10 (0.77, 1.57)	1428	587	0.33	1.11 (0.81, 1.51)
Female	146	53		1.00	158	75		1.00
Age at diagnosis								
35 and under	635	239		1.00	701	348		1.00
35+	776	219	0.01	1.37 (1.09, 1.71)	885	314	<0.001	1.50 (1.23, 1.82)
Race/ethnicity								
Black (non-Hispanic)	511	206	<0.001	0.60 (0.45, 0.80)	578	299	<0.001	0.70 (0.55, 0.90)
Hispanic	434	136	0.67	0.87 (0.64, 1.16)	496	190	0.23	0.95 (0.74, 1.22)
Other	43	9	0.22	1.29 (0.60, 2.77)	47	14	0.26	1.18 (0.62, 2.24)
White (non-Hispanic)	423	107	--	1.00	465	159	--	1.00
Homeless at diagnosis								
Yes	22	31	<0.0001	0.26 (0.15, 0.45)	32	48	<0.0001	0.27 (0.17, 0.43)
No	1389	427		1.00	1554	614		1.00
CD4 count at diagnosis								
<200	236	96	0.04	0.72 (0.55, 0.95)	244	162	<0.0001	0.52 (0.41, 0.66)
≥200	1175	362		1.00	1342	500		1.00
Time to linkage								
Within 30 days	1291	422	0.66	0.96 (0.64, 1.42)	1438	599	0.89	1.05 (0.76, 1.44)
After 30 days	129	36		1.00	148	63		1.00
Site of diagnosis								
Partner Site	907	310	0.18	0.92 (0.72, 1.16)	1051	458	0.18	0.91 (0.74, 1.12)
AHF Site	504	148		1.00	535	204		1.00
Region of diagnosis								
California	770	270	0.10	0.84 (0.66, 1.09)	875	363	0.88	1.05 (0.85, 1.31)
Other States	641	188		1.00	711	299		1.00
Season of diagnosis								
Winter	411	145	0.30	0.90 (0.71, 1.14)	459	210	0.19	0.87 (0.71, 1.07)
Non-winter	1000	313		1.00	1127	452		1.00
Year of diagnosis								
2012	479	203		1.00	542	279		1.00
2013	932	255	<0.0001	1.57 (1.24, 1.97)	1044	383	<0.001	1.50 (1.23, 1.84)

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CHAPTER 3

Association and Predictive Accuracy of Differing Retention Measures with HIV Viral Suppression: A Statistical Learning Approach

3.1 ABSTRACT

Background: Viral suppression is the goal of care for persons living with HIV (PLHIV). Maintenance of undetectable levels of viral load leads to more favorable health outcomes and normal expected lifespans. The HIV care continuum (or cascade) is commonly used as a model to achieve the end goal of viral suppression. The most difficult continuum stage to measure is retention in care. Multiple definitions for retention in care exist without an established gold standard. This study evaluated eight different measures of retention among clients from a national non-profit HIV care organization for: 1) association between retention measures and with viral suppression, and 2) predictive accuracy for viral suppression.

Methods: Administrative and HIV testing data were extracted for all HIV-positive clients referred for care between January 1, 2012 and December 31, 2013 at a national non-profit HIV care organization. Eight different measures of retention were derived for each client as well as viral load status at one year. Spearman's rank correlation coefficients were used to assess relationships between the retention measures. Probability of one-year viral suppression was modeled for each retention measure with logistic regression. K-folds (k=10) cross validation (cv) was used to assess the relative accuracy of each retention measure in predicting viral suppression.

Results: During the two-year study period, 3,229 clients were referred for care and included in analyses. Retained status ranged from 59.2% to 78.8% depending on the retention measure. Distribution of baseline covariates were similar across the retained groups. Retention measures based on the same elements (either kept visits or missed visits) were more highly correlated (r range from -0.51 to -0.86 and 0.78 to 0.94) than across elements (r range -0.30 to 0.23). Each retention measure was significantly associated with viral suppression (OR range from 0.30 to 0.75 and 2.12 to 3.96). CV prediction accuracy for the retention measures were between 59.14% and 66.58%, but the rank order of the measures differed with regards to odds ratio and predictive accuracy.

Conclusion: The retention measures are all associated with viral suppression although the ordering of the strength of association differs from that of the previous retention measure studies. Thus, when possible, retention measures should be evaluated with regards to the population and the desired goals. Further, methods that can evaluate the generalized performance of fitted models (eg. cross validation) should be considered in addition to traditional fit statistics in determining the most appropriate retention measures. In this population, the highest prediction accuracy was observed for the four-month visit constancy measure. Composite measures or use of multiple retention measures together may also provide more accuracy in predicting viral suppression. A universal gold standard may not exist, but with evaluation specific to a population, current retention measures can be valuable prognostic tools for viral suppression.

Keywords: HIV Care Continuum; viral suppression; retention; K-folds; cross-validation; statistical learning

3.2 INTRODUCTION

Viral suppression is the goal of care for persons living with HIV (PLHIV). HIV-positive individuals who maintain undetectable levels of viral load reduce their probability of transmission, can remain asymptomatic, and have expected lifespans comparable to that of the general population.[1-6] The HIV care continuum (or cascade) is commonly used as a model to achieve the end goal of viral suppression.[7] HIV management programs focus on achieving each stage of the continuum with a natural assumption that it will aid in progressing to the next subsequent step until eventual viral suppression. Thus, for programs based on the HIV care continuum model, their overall success will be influenced by the quality and appropriateness of the definitions used for the continuum stages.

Perhaps the most difficult continuum stage to measure is retention in care.[8] Multiple definitions of retention exist and can vary with regards to the relevant window of time and/or type of visit specified (eg. HIV care visits, HIV laboratory tests). Despite the numerous definitions, the common goal of the various retention measures is to represent engagement in HIV care in a discrete or quantifiable manner. It is well-established that sustained engagement in care is critical for viral suppression and improved overall health outcomes.[9-12] Thus, the challenge in defining retention is to do so in a way that adequately portrays engagement in care.

The key elements of the various measures of retention involve HIV care visits (either kept or missed), with each retention definition, in essence, being a specified algorithm of visits. HIV testing information (viral load or CD4 count) has also been used as a proxy in lieu of actual provider visit records when administrative information from HIV providers may not be readily available.[13] National estimates of retention by the Centers for Disease Control and Prevention (CDC) and other studies have used laboratory-based visit information.[14-16] Additional

information on appointments in combination with visit information can also provide the extra dimension of adherence to the retention measure.

Although no gold standard for retention has been established, positive associations between retention and viral suppression persist regardless of the definition used.[10,16,17] Previous studies have compared different retention measures within the same population with regards to association with viral suppression and correlations between the measures. These retention measures were similarly associated with viral suppression and other demographic information. Further, there was some degree of correlation between the measures, with the highest correlations among measures based on similar attributes.[10,18] Given these findings, the question arises as to whether the various retention measures differ in utility for any given population.

Similar comparison of these retention measures in another setting would provide further insight into whether the relationships between the measures themselves and with viral suppression would differ depending on the study population. Also, if the retention measure is to serve as a prognostic tool for viral suppression, then the measures that would best predict viral suppression in new patients would be preferable. This study addresses both issues by evaluating several different existing retention measures in a population of clients from a national non-profit HIV care organization. Associations with viral suppression controlling for demographic covariates are examined. Further, novel to our approach is the application of statistical learning methods that estimate the predictive accuracy of fitted models when applied to new data.[19]

3.3 METHODS

Study Population

Study information was obtained from a centralized data system serving all AIDS Healthcare Foundation (AHF) sites in the United States. These sites served multiple regions including California, District of Columbia, Florida, Georgia, Michigan, Nevada, North Carolina, New York, Ohio, Pennsylvania, and Texas. Initial study inclusion were all clients diagnosed with HIV (either at AHF or a partner site) and referred to AHF for care from January 1, 2012 through December 31, 2013. Clients with a missing date of HIV diagnosis were excluded. Clients with no documented viral load following referral were also excluded as their viral status could not be determined.

HIV Retention Measures

Eight different measures of retention (listed below) were created from provider visit/appointment information and laboratory testing information. Consistent with previous studies, only scheduled visits with primary HIV medical care providers were considered for the measures. Six of the retention measures in this study were evaluated in at least one of the retention measure studies previously mentioned.[10,18,20] Two additional commonly used retention measures (NCQA, CDC) were also included in our study.

1) National Committee for Quality Assurance (NCQA) defined retention – 2 or more clinic visits by ≥ 60 days in the year following HIV diagnosis (dichotomous measure, yes/no)[21,22]
2) CDC defined retention – 2 or more viral load or CD4+ tests separated by ≥90 within 1 year of HIV diagnosis (dichotomous measure, yes/no)[14]
3) Missed visits (count) – number of missed visits accrued over 1 year from HIV diagnosis (count measure)

4) Missed visits (dichotomous) – yes/no dichotomous variable for any missed visits within 1 year of HIV diagnosis (dichotomous measure, yes/no)
5) Visit adherence – proportion of (kept visits / scheduled visits) within 1 year of HIV diagnosis (continuous measure, range 0.0-1.0)
6) 4-Month visit constancy – number of 4 month intervals with at least one kept visit within 1 year of HIV diagnosis (categorical measure, range 0-3)
7) 6-Month gap – ≥189 days elapsed between sequential kept visits within 1 year of HIV diagnosis (dichotomous measure, 'no'=retained)
8) Health Resources & Services Administration, HIV/AIDS Bureau (HRSA HAB) defined measure – 2 kept visits separated by ≥90 within 1 year of HIV diagnosis (dichotomous measure, 'yes'=retained)[10]

Covariates and Outcome

Covariates were included and categorized based on previous literature and separate analyses involving the same study population. Gender in this study refers to the gender of the client specified at birth. Age was dichotomized into two categories, 35 years or younger, and older than 35, based on previous literature and the distribution of the sample (described below).[23-25] Race/ethnicity was represented by the indicator variables: Black (non-Hispanic), Hispanic, and Other ethnicity, with White (non-Hispanic) as the reference. Homeless indicates the self-reported housing status of the client. Low CD4 count refers to a CD4 count below 200 copies/μL with any higher CD4 count as the reference.[26] Partner-site of diagnosis indicates whether the client was diagnosed and referred by a non-AHF site. California (versus any other state) reflects the location of the diagnosing site, as approximately half of the client population was from California. All covariates were measured at baseline.

The primary outcome variable was viral suppression (≤ 200 copies/mL) at one year following HIV diagnosis. Viral suppression was based on the VL measurement closest in date to exactly one year post-diagnosis including measurements up to 120 days after the one-year mark. The additional 120-day window provides more information upon which to best estimate the one-year viral status.[10]

Study Analyses

Descriptive statistics including frequencies and means were used to summarize the retention measures and baseline covariates. To assess the relationships between retention measures, Spearman rank correlation coefficients were generated. The associations between the retention measures and the outcome of viral suppression, were evaluated with logistic regression. All retention measures were modeled as dichotomous variables except for missed visit counts, visit adherence proportion, and four-month visit constancy. Missed visits (count) was included as an integer value in the models, ranging from 0 to 4 with 4 representing four or more missed visits. Four-month visit constancy was also modeled as an integer value from 0 to 3. Visit adherence (proportion) was entered as quartiles with a separate category for 100% adherence (five categories total). To assess the ability of the retention measures to predict viral suppression, the full model for each retention measure was evaluated using K-folds (k=10) cross validation (cv).[19] In contrast to traditional statistical methods, a statistical or machine learning method such as cross validation helps us evaluate how well a model would perform in predicting a target outcome (viral suppression in this case) in new data. Cross validation estimates performance by fitting the model to only a select portion of the data (training data) and then applying that model to the unfitted portion of data (test data). This process provides the error rate of the fitted model in predicting outcome in the test data. One minus the error rate then

provides the estimated prediction rate for each retention measure adjusting for the same covariates. All analyses were performed with complete case. For univariate analyses, chi-square p-values were reported. K-folds cross validation was performed with R v3.3.2 (The R Foundation for Statistical Computing, Vienna, Austria). All other analyses were conducted with SAS *v*9.4 (SAS Institute, Cary, North Carolina, USA).

3.4 RESULTS

Baseline Characteristics

Data from 3,229 clients were included in the analyses from the two-year study period. (Table 3-1) However, for analyses involving the two retention measures with an adherence component (missed visits and visit adherence), only clients with a scheduled appointment on record (n=2,834) were included. The clients were predominantly male at birth (88.7%) with over 90% of male clients identifying as men who have sex with men (not shown). Mean age was 36.9 years with a median of approximately 35 (50.2% over age of 35). Black (non-Hispanic) was the largest race/ethnic group (41.0%). Unstable housing status (homeless) was reported in 3.9% of the clients. Low baseline CD4 count (<200 cells/μL) was observed in 16.7% of population. The majority of clients (60.0%) were diagnosed with HIV at non-AHF site (partner site) before being referred to AHF. Approximately half of clients (50.5%) were diagnosed at a California site.

Retained status among the retention measures ranged from 59.2% (CDC retention) to 78.8% (six-month gap). (Table 3-1 and 3-2) Compared to overall, retained clients tended to be older with higher mean age and proportion over age 35. The proportion of Black (non-Hispanic) clients (lower than overall), White (non-Hispanic) clients (higher), and homeless status (lower) among the retained group were also slightly different than the overall population.

Spearman Rank Correlation among Retention Measures

The estimated Spearman rank correlation coefficients were highest between retention measures based on similar definitions. (Table 3-3) Retention measures based on timing of two or more visits (NCQA, HRSA, CDC) ranged from 0.78 to 0.94. Measures based on visits throughout the year (four-month visit constancy, six-month gap) showed moderate correlation (-0.65) with each other. Correlations between measures with an adherence component (missed visits count, missed visits dichotomous, visit adherence) were also high (range -0.81 to -0.86). Moderate to high correlations were observed when comparing the "two or more visits" measures (NCQA, HRSA, CDC) to six-month gap (range -0.51 to -0.56) and four-month visit constancy (range 0.81 to 0.86). The lowest correlations occurred when adherence-based measures (count and dichotomous missed visit, visit adherence) were compared to any other retention measure (range between -0.10 to 0.32).

Associations and Predictive Accuracy with Viral Suppression

The retention measures were each significantly associated with viral suppression, both crude and adjusted. (Table 3-4) Six-month gap (adjusted odds ratio (AOR)=0.30; 95% Confidence Interval (CI) 0.21-0.43), missed visits dichotomous (AOR=0.50; 95% CI 0.38-0.66) and missed visits count (AOR=0.75; 95% CI 0.69-0.81) were inversely associated with viral suppression. Positive associations with viral suppression were observed for the other retention measures: visit adherence (AOR=2.12; 95% CI 1.79-2.50), four-month visit constancy (AOR=2.27; 95% CI 1.81-2.85), HRSA (AOR=2.94; 95% CI 1.48-5.86), CDC (AOR=3.46; 95% CI 2.42-4.97), and NCQA (AOR=3.96; 95% CI 1.83-8.58). The cv prediction accuracy for retention measure models were all above 50% accuracy, ranging from 59.1% (missed visits dichotomous) to 66.6% (four-month visit constancy). (Table 3-4) CV prediction accuracy for the

other six retention measure models were between 62.5% (HRSA) and 65.3% (six-month gap). The cv prediction accuracy reflects the estimated percentage of correctly predicted outcomes when a fitted model is applied to new data. The order of magnitude for odds ratios was different than that for cv prediction accuracy.

3.5 DISCUSSION

This study was able to evaluate the six retention measures from the two previous retention measure studies as well as two additional measures. Similar to both prior studies, the measures were evaluated in a single population allowing for a standardized comparison. Further, this is the first comparison that has been able to incorporate information from three key elements: kept visits, missed visits, and HIV laboratory tests. It has been suggested that the use of HIV laboratory tests in lieu of provider visits (eg. CDC measure) may misclassify individuals with regards to retention status.[20] So, our utilization of HIV laboratory test information provided an opportunity to compare the performance of the CDC retention measure with the equivalent measure based on provider visits, HRSA. Associations with the covariates were not examined, but previous analyses on these same data for the CDC retention measure showed only slight associations with age, CD4 count, and homelessness, which is consistent with the covariate distribution among our retained groups. (Table 3-1)

Correlations between the retention measures existed in a specific pattern. As expected, retention measures based on the same element (kept visits or missed visits) were highly associated with one another. The CDC and HRSA retention measures both showed correlations with other measures in a similar manner, supporting the appropriateness of HIV tests as a proxy of provider visits. However, there was little correlation between measures across the element

groupings, unlike a previous study that observed moderate associations.[10] This finding suggests that the more important variant of information is the element used rather than the actual configuration of the measure. Both elements provide different information regarding engagement in care. Thus, the best representation of engagement in care may involve use of both kept and missed visits.

As expected, each retention measure was significantly associated with viral suppression. To their credit, the cv prediction accuracy for each retention measure model was also over 50%. However, the rank order of the retention measures with regards to odds ratio magnitude differed from that of cv prediction accuracy. This contrast is not surprising given that statistical measures of association such as odds ratios do not necessarily reflect the ability to accurately classify a future event.[27] Further, odds ratios are based on models evaluated with the entire dataset which minimizes model fit error for the given data but not for new data. Thus, despite the associations with viral suppression, determining which measure would best predict viral suppression in a new patient cannot be determined by odds ratios alone. The observed associations and prediction accuracy also suggest that both kept visits and missed visits are significant determinants of viral suppression, which further supports the notion that the use of multiple retention measures together may be preferable. For example, a model with the two retention measures least correlated (missed visit count and four-month visit constancy) produced a higher cv prediction accuracy (68.7%) than that of any retention measure alone. Future research could focus on the most effective combination of components for identifying targets of intervention. Components may include current retention measures as well as composites that may also involve broader longitudinal aspects. Machine learning techniques such as cross validation, which are increasingly accessible due to advances in computing power, can be valuable tools in this area.

Individually, the highest cv prediction accuracies were observed for four-month visit constancy and six-month gap, followed by the measures based on the temporal spacing of kept visits: CDC, NCQA, and HRSA. It appears that the broader the time span reflected in the measure translates to more accurate prediction of viral suppression. The order of predictive accuracy for these measures is not surprising since previous literature suggest that longitudinal retention measures may more accurately capture the true state of engagement in care.[28] Further, the broader time frames may also be more reflective of long-term HIV viral status monitoring which is associated with improved ART adherence.[29] The two other ordinal measures (missed visit count and visit adherence), other than four-month visit constancy, also showed high cv prediction accuracy. The higher fidelity of information provided by the multiple levels in these ordinal measures likely contribute to their high predictive accuracy. Conversely then, it follows that the lowest cv prediction accuracy was observed in the one retention measure (dichotomous missed visit) with no time component or gradation of information.

Although the cv prediction accuracy for the ordinal retention measures is high, the interpretation of the ordinal measures is not intuitive. From a client management perspective, to simply state that clients should have less missed visits or maintain higher visit adherence is ambiguous and may lead to inconsistent standards. A sub-analyses (not shown) with dichotomized versions of the ordinal retention measures separated at each level of the measure showed that cv prediction accuracy varied by level. For example, within the visit adherence measure, the highest cv prediction accuracy was observed at the 75% visit adherence level (above versus below). The highest cv prediction accuracy for dichotomized versions of missed visit count occurred at three or more missed visits versus less than three missed visits. The level of four-month visit constancy with the highest cv prediction accuracy was for kept visit(s) at all

three four-month intervals versus anything less. Evaluating each level within the ordinal measure shows that indeed certain levels may be more impactful than others and provides more exact standards that should be reached to best achieve viral suppression. It is important to note that the cv prediction accuracy reported is for that of the full model. Thus, the prediction accuracy should not be interpreted as the absolute prediction percentage of each retention measure alone for any given client. Rather, the cv prediction accuracy in our study allows for a relative comparison of the different retention measures.

There are limitations in this study including generalizability. The clients in our study population were mostly male and, of the men, over 90% men who have sex with men (MSM). Further, many clients diagnosed at AHF were also regular wellness clients prior to HIV diagnosis. Considering adherence to ART is a major component of viral suppression, individuals health-conscious enough to maintain regular wellness visits may operate under a different dynamic with regards to retention and viral suppression. Another issue is possible survivor bias from our definition of one-year outcome. To be included in analyses, clients must have had a viral load measurement within the designated window of time at one-year post-diagnosis. This requirement precludes clients that were lost to follow-up through migration, death, or any other reason. If the factor(s) influencing follow-up were related to retention and viral suppression, then the results may not accurately represent the entire study population. Although this method allows for inclusion of more clients in analyses, it also leads to higher potential for misclassification of the true viral state due to random laboratory errors or viral blips.[30,31] However, considering the consistency of the associations and cv prediction accuracy, this possible bias may not have drastically impacted results.

Conclusion

Our analyses of these eight different retention measures has provided insight on: 1) the associations between the measures themselves and with viral suppression, and 2) the consistency of these relationships between different populations. Similar to the previous retention measure studies, the state of being retained according to each definition was associated with higher probability of viral suppression. Also consistent with this prior literature, correlations between retention measures depended on the element (kept visits or missed visits) used – correlations between measures based on the same element were consistently higher than between measures based on different elements. CV predictive accuracy for the retention measures were all over 50%. However, the degree of predictive accuracy did not follow the same order as for the strength of association (odds ratio). This discrepancy suggests that traditional model fit statistics alone may not best indicate the ideal retention measure. Rather, machine learning methods that can evaluate the generalized performance of a model may more effectively determine the measure most in line with clinical management objectives. Application of these methods in this population showed that the four-month visit constancy retention measure would be the most accurate predictor of viral suppression among new patients. Focus on this measure in future research can clarify the universality of its prediction accuracy. Component-wise, both kept visits and missed visits provide important but different information relevant to viral suppression, based on the inter-measure correlations, odds ratios, and cv prediction accuracy observed. As such, for program management purposes, multiple measures or a composite measure that incorporates both elements (kept visits and missed visits) may be more ideal for guiding performance goals.

Overall, when comparing our results with those of prior retention measure studies, the similarities (correlations between retention measures, and positive associations with viral suppression) and differences (ordering of strength of associations, and predicative accuracy)

suggest that perhaps no universal gold standard exists for retention measures. Rather, current retention measures are each valuable and emphasize the significance of maintaining some degree of engagement in care. When possible, populations should be individually analyzed to determine the retention measure most optimal for achieving specified goals.

TABLES

Table 3-1. Baseline Characteristics by Retention Measure among HIV-positive clients at a national non-profit HIV care organization, 2012-2013

	Overall (%) N=3,229	NCQA (%) (Retained; n=2,247)	CDC (%) (Retained; n=1,914)	Missed Visits (%) (Zero Missed; n=890)	Four-month Visit Constancy (%) (≥2; n=2,090)	Six-month Gap (%) (No Gap; n=2,543)	HRSA (%) (Retained; n=2,158)
Male at birth	88.7	89.4	89.5	90.1	89.5	89.3	89.7
Mean age (standard dev.)	36.9 (11.5)	37.5 (11.4)	37.8 (11.4)	39.3 (11.8)	37.6 (11.4)	37.3 (11.5)	37.5 (11.4)
Age 35+	50.2	52.4	53.2	58.5	52.9	51.3	52.6
Race/ethnicity							
Black (non-Hispanic)	41.0	39.3	38.2	32.0	39.0	40.2	39.1
Hispanic	29.3	29.9	30.5	32.4	29.7	29.9	29.7
Other Ethnicity	2.9	2.7	2.2	3.8	2.7	2.7	2.7
White (non-Hispanic)	26.8	28.1	29.1	31.8	28.6	27.2	28.5
Homeless	3.9	3.0	2.8	1.7	2.4	3.3	2.9
CD4 count < 200 copies/µL	16.7	17.0	17.8	15.0	17.2	16.5	17.1
Diagnosed in Outreach/Partner Si	60.0	65.9	65.1	62.3	65.4	64.7	65.6
Diagnosed in California	50.5	54.7	55.1	50.8	54.6	52.6	54.8

Table 3-2. Retention Measure Status among HIV-positive clients at a national non-profit HIV care organization, 2012-2013

	Overall (%) N=3,229
NCQA (Retained)	69.6
CDC (Retained)	59.3
Missed Visits (Count)	
Zero	31.4
One	26.7
Two	17.5
Three	10.1
Four or more	14.3
Missed Visits	
Zero	31.4
One	26.7
Two	17.5
Three	10.1
Four or more	14.3
Visit Adherence	
0-24%	4.2
25-50%	5.1
51-74%	15.4
75-99%	43.9
100%	31.4
Four-month Visit Constancy	
Zero	15.8
One	19.4
Two	17.3
Three	47.5
Six-month Gap (no gap)	78.8
HRSA (Retained)	66.8

Table 3-3. Spearman Rank Correlation Coefficients by Retention Measure among HIV-positive clients at a national non-profit HIV care organization, 2012-2013

	NCQA	CDC	Missed Visits (Count)	Missed Visits (Dichotomous)	Visit Adherence	Four-month Visit Constancy	Six-month Gap	HRSA
NCQA	1	0.78	0.09	-0.02	0.23	0.83	-0.56	0.94
CDC	0.78	1	0.04	-0.04	0.23	0.81	-0.51	0.83
Missed Visits (Count)	0.09	0.04	1	0.84	-0.81	-0.01	0.07	0.09
Missed Visits (Dichotomous)	-0.02	-0.04	0.84	1	-0.86	-0.10	0.13	-0.03
Visit Adherence	0.23	0.23	-0.81	-0.86	1	0.32	-0.30	0.23
Four-month Visit Constancy	0.83	0.81	-0.01	-0.10	0.32	1	-0.65	0.86
Six-month Gap	-0.56	-0.51	0.07	0.13	-0.30	-0.65	1	-0.53
HRSA	0.94	0.83	0.09	-0.03	0.23	0.86	-0.53	1

Table 3-4. Association and Predictive Ability of Retention Measures for Viral Suppression among HIV-positive clients at a national non-profit HIV care organization, 2012-2013

	Univariate *p* value	Multivariate Odds Ratio (95% CI)	CV Prediction Error (%)	CV Prediction Accuracy (%)
NCQA	<0.0001	3.96 (1.83, 8.58)	36.85	63.15
CDC	<0.0001	3.46 (2.42, 4.97)	35.95	64.05
Missed Visits (Count)	<0.0001	0.75 (0.69, 0.81)	34.95	65.05
Missed Visits (Dichotomous)	<0.0001	0.50 (0.38, 0.66)	40.86	59.14
Visit Adherence	<0.0001	2.12 (1.79, 2.50)	36.18	63.82
Four-month Visit Constancy	<0.0001	2.27 (1.81, 2.85)	33.42	66.58
Six-month Gap	<0.0001	0.30 (0.21, 0.43)	34.67	65.33
HRSA	<0.0001	2.94 (1.48, 5.86)	37.47	62.53

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CHAPTER 4

Does sexual behavior change following two significant events in the course of HIV infection: linkage to HIV care and initial viral suppression?

4.1 ABSTRACT

Background: Almost 50,000 individuals are newly infected with HIV annually in the United States. Sexual contact continues to be the primary mode of HIV transmission attributing to over 90% of new cases. Thus, reducing high-risk sexual behaviors is important for HIV prevention. A goal of early intervention programs (EIP) for HIV is to reduce further transmission from persons newly diagnosed with HIV. However, current knowledge on the dynamics of sexual behaviors following linkage to HIV care and further is mixed. This study will evaluate change in sexual behavior using sexually transmitted disease (STD) infection as proxy through two life events: 1) linkage to HIV care; and 2) initial viral suppression.

Methods: Demographic, administrative, and STD/HIV testing information were extracted for clients referred to a national non-profit HIV care organization between January 1, 2012 and December 31, 2013. Prevalence of STD was compared for the following: 1) one year prior to linkage versus one year after linkage; and 2) period between linkage and initial viral suppression versus the equivalent length of time (days) after initial viral suppression. McNemar's test of paired proportions was used to assess overall prevalence between the pre and post-periods. The probability of sexual behavior change given pre-period STD status and other demographic covariates was modeled with multivariate logistic regression.

Results: A total of 173 and 227 clients met all criteria for inclusion in the pre/post linkage and initial viral suppression analyses, respectively. Overall prevalence of STD infection was significantly lower (p=0.03) in post-linkage versus pre-linkage periods. The presence of a STD in the pre-period was associated with change in sexual behavior for both the linkage (AOR=14.92, 95%CI=6.41, 34.76) and viral suppression groups (AOR=16.80, 95%CI=7.15, 39.48). In the model restricted to clients with a STD in the pre-linkage period, Hispanic ethnicity was significantly associated with a decrease in high-risk sexual behaviors (AOR=12.74, 95%CI=1.61, 100.72) while non-Hispanic Whites were less likely to show such change.

Conclusion: Overall, for both the linkage and viral suppression groups, clients with a STD in the pre-period were more likely to change their STD status in the post-period than clients with no STD in the pre-period. Reduction in STD prevalence from pre to post-linkage may be due to influence of HIV diagnosis on sexual behaviors. Initial viral suppression does not appear to be associated with any further change in sexual behaviors. Change in behaviors differed by racial/ethnic group with non-Hispanic Whites with pre-linkage STD less likely to change sexual behaviors and to achieve timely viral suppression. Identification of these types of subgroups within the broader analyses would contribute to HIV prevention and wellness efforts.

Keywords: High-risk sexual behavior; sexually-transmitted disease; linkage; viral suppression; sexual behavior change

4.2 INTRODUCTION

In recent years, almost 50,000 individuals in the United States are still newly infected with HIV annually. The dominant mode of transmission continues to be sexual contact with over 90% of new HIV infections attributable to either same-sex or heterosexual encounters.[1] Different types of sexual practices vary with regards to the HIV transmission risk. Whether during same-sex or heterosexual contact, the highest HIV transmission risk per act involves unprotected receptive anal intercourse, with insertive anal intercourse and penile-vaginal intercourse several folds lower in risk.[2] Regardless of sexual act, HIV transmission risks can be drastically reduced by condom use.[2,3]

These same sexual practices are also related to the spread of other sexually transmitted diseases (STD) as both HIV and STDs can share similar modes of transmission.[4] Untreated bacterial STDs on their own can pose health issues related to infertility, pelvic inflammatory disease, and other long-term health complications.[5] Concurrent STD infection in HIV-positive individuals or STD infection in individuals without HIV can both increase the risk of HIV transmission.[6-9] Conversely, treatment of STDs in HIV-positive individuals may reduce the probability of further HIV transmission.[10] Given the impact of STDs alone and in the context of HIV prevention, it is important then to understand whether the frequency of engaging in high risk sexual behaviors changes following HIV diagnosis and to identify factors associated with such changes.

Early intervention programs (EIP) for HIV focus on linkage to care along with HIV prevention education and counseling. The end goal of these programs is to provide individuals a path to eventual viral suppression for the overall well-being of the HIV-positive individual as well as for his/her network through reduced transmission. The

prevalence of high-risk sexual behaviors is believed to decrease following HIV diagnosis.[11] Further, studies have also observed declines in risky sexual behavior among those adhering to HIV treatment and those reaching viral suppression.[12-15] Given these findings and the intent of EIP, a natural assumption may be that HIV-positive individuals who have been linked to HIV care would reduce any existing high-risk sexual behavior. However, there are reasons to suggest that high-risk sexual behaviors may actually increase following linkage and initiation of ART therapy. Beliefs about reduced HIV infectiveness from HAART treatment and low viral loads have been associated with increase in certain sexual risk behaviors.[16-22] Thus, understanding the effects of being introduced to HIV care (linkage) and the ongoing treatment on the dynamics of sexual behaviors is important in the context of HIV prevention.

Comparing the prevalence of high risk sexual behaviors in HIV-positive individuals in the time frames prior to and following HIV diagnosis would provide insight on the direction of any sexual behavior change. Further, evaluation of demographic characteristics associated with any change would provide basis for more targeted behavioral interventions, which has been mathematically shown effective.[23] The current study investigated these issues in a population of HIV-positive clients linked to care at a national non-profit HIV care organization.

4.3 METHODS

The study population was derived from all clients referred to AIDS Healthcare Foundation (AHF) for linkage and care between January 1, 2012 and December 31, 2013. Clients were initially diagnosed with HIV either at an AHF site or an external partner site.

Administrative and laboratory testing information were extracted from a centralized data system serving all national AHF sites, which includes locations in the states of California, District of Columbia, Florida, Georgia, Michigan, Nevada, North Carolina, New York, Ohio, Pennsylvania, and Texas. A subset of clients with at least one documented test and result for Chlamydia or gonorrhea, or at least two separate rapid plasma regain (RPR) titers for syphilis in each of the time frames being compared were then selected from the initial HIV client population. Clients with missing date of HIV diagnosis were excluded.

Two comparisons of the prevalence of high-risk sexual behaviors between different time frames were conducted: 1) one year preceding linkage to care for HIV versus (pre-linkage) one year following linkage to care (post-linkage); and 2) period from date of linkage to initial viral suppression (pre-VS) versus the equivalent length of time (in days) following initial viral suppression (post-VS). The presence of a new STD infection based on STD test results was used as a proxy for high-risk sexual behaviors. Consecutive positive tests for Chlamydia or gonorrhea were at least 60 days apart to be considered separate disease incidences. A new infection of syphilis was based on a four-fold increase between two or more RPR titer values. Practice of high-risk sexual behavior was designated a yes/no for each time frame of interest. A "yes" was based on any new STD infection in that time frame. A "no" was designated if only negative STD test results were documented in the time frame. If no valid STD test results were available for a given time frame, then high-risk sexual behavior was considered unknown, and the client was excluded from analyses involving that time frame.

Linkage to HIV care was based on the definition by the Centers for Disease Control and Prevention (CDC). A client was considered linked if there was a laboratory record of at least one viral load or CD4+ measurement within 90 days of the HIV diagnosis date. Initial viral

suppression was determined by the earliest documented viral load measurement of ≤ 200 copies/mL within one year of HIV diagnosis. If there were no such viral load measurements within the year, then that client was not included in analyses involving initial viral suppression.

Covariates were categorized according to previous literature and analyses involving the same client population. Baseline age was dichotomized into 35 years of age or less versus over 35 years. Race/ethnicity was modeled as indicator variables for Black (non-Hispanic) and Hispanic, with White (non-Hispanic) and Other as the reference. Low CD4 indicates a baseline CD4 count of below 200 copies/μL. Partner site refers to the client having been diagnosed and referred from a site external to AHF. California site of diagnosis represents the client's diagnosing site being within the state of California as opposed to any other state.

Descriptive statistics were used to summarize the baseline covariates and prevalence of new STD infection. McNemar's test for paired data was used to compare the STD prevalence between the pre and post periods. For both comparisons, logistic regression was used to model the probability of sexual behavior change given new STD status in the pre-period. Sexual behavior change was considered to have occurred if the presence of a new STD infection differed between the pre and post time frames (either no new STD in the pre-period with a new STD in the post-period, or vice versa). If there was no difference in new STD infection between the time frames (either the presence or lack of a new STD infection in both pre- and post-periods), then sexual behavior did not change. Missing data were excluded from analyses. All analyses were performed with SAS *v*9.4 (SAS Institute, Cary, North Carolina, USA).

4.4 RESULTS

A total of 173 and 227 clients met all criteria for inclusion in the pre/post linkage and initial viral suppression analyses, respectively. (Table 4-1) Both groups of clients are almost exclusively men and as a result, gender was not included as a covariate in the logistic modeling. Mean age and proportion over 35 years of age were similar in both groups. Black (non-Hispanic) and Hispanic ethnicity comprised a slightly higher percentage of clients in the viral suppression group (31.3% Black and 38.8% Hispanic) than the linkage group (26.0% Black and 38.2% Hispanic). Clients in both groups were also similar with regards to low baseline CD4 count (<200 copies/μL) and diagnosing site within California. However, a larger proportion of the viral suppression group were referred from a non-AHF partner site (48.5% versus 35.3%). Overall prevalence of new STD infection in both pre and post periods were higher in the linkage group (32.4% pre and 22.0% post) than in the viral suppression group (21.6% pre and 18.9% post).

Although overall prevalence of new STD infection decreased in the post-periods for both groups, the change was significant only for the linkage group (McNemar's test p-value of 0.03). (Table 4-2) For the linkage group, prevalence of new STD infection decreased from 32.4% (pre-linkage) to 22.0% (post-linkage). Among the initial viral suppression group, the STD prevalence was 21.6% (pre-VS) and 18.9% (post-VS) without a statistically significant difference.

Odds ratios for sexual behavior change (SBC) from multivariate logistic regression are shown in table 4-3 (linkage group) and table 4-4 (viral suppression group). Among the linkage group, the odds of clients reducing their high-risk sexual behavior was greater than the odds of clients adopting high-risk sexual behaviors following linkage (STD+pre in overall linkage model: adjusted odds ratio (AOR)=14.92; 95% Confidence Interval (CI) 6.41-34.76). In the

model restricted to STD+ in the pre-linkage period, Hispanic ethnicity was significantly associated with a decrease in high-risk sexual behavior (AOR=12.74, 95% CI 1.61-100.72).

In analyses for the initial viral suppression group, low CD4 count was excluded from the model with pre-VS STD due to sparse data. Similar to that observed in the linkage group, the odds of reducing high-risk sexual behavior following initial viral suppression was significantly greater than the odds of starting high-risk sexual behavior (STD+pre in overall viral suppression model: AOR=16.80; 95% CI 7.15-39.48). No other associations were statistically significant at the 0.05 level in the viral suppression models.

4.5 DISCUSSION

In the pre/post linkage comparison, the prevalence of new STDs significantly decreased from the pre-linkage to the post-linkage period. In contrast, new STD prevalence remained similar from the pre-VS to post-VS periods. However the STD prevalence in both the pre-VS and post-VS periods were still at least six percentage points lower than that of the post-linkage group. These results are more supportive of the aforementioned literature on an association between decreased high risk sexual behavior and ART adherence/viral suppression, instead of an increase or continuation of these high-risk behaviors due to "HAART complacency". This reasoning is not to suggest the complete lack of treatment complacency, but rather, that any influence from this phenomenon may not always override factors with influence in the other direction. Even with the effect of treatment complacency present, it has been suggested that actual increase in high risk sexual behaviors due to treatment complacency only occurs in a minority of individuals and as such, is not a major attributable factor in HIV transmissions.[24,25] Instead, the significant decrease in STD prevalence observed after linkage may result more from

the tempering influence of HIV diagnosis on high-risk behaviors.[11] This reduction in high-risk sexual behaviors following HIV diagnosis has also been noted to be stable for at least one year[26], which is reflected in the overall lower and consistent STD prevalence observed in the pre and post-VS periods.

In the logistic regression models, the odds ratios for the covariate, STD infection (pre-period), were significant and positive for both the linkage and viral suppression analyses. Stated another way, clients who were STD-positive in the pre-periods were more likely to be STD-negative in the post-periods than vice versa (STD-negative in pre-period becoming STD-positive in post-period). However, in the linkage group, it is interesting to note that STD prevalence in the post-linkage period was higher among clients with no pre-linkage STD than those with a pre-linkage STD. Although the post-linkage STD prevalence for both were still lower than overall pre-linkage STD prevalence, the higher post-linkage STD prevalence among clients initially without STD suggests that previous STD history may influence future risky sexual behavior, more so than linkage to HIV care in this case. More comprehensive information on STD history and testing results outside of AHF would be needed to clarify this possibility.

Hispanic ethnicity was also associated with a decrease in high risk sexual behavior following linkage. And although not significant at the 0.05 level, the odds ratio for Black ethnicity for this same association was high at 3.14. These observations indicate that the reference group (White non-Hispanic) for ethnicity must be at relatively higher risk of STD infection in the post-linkage period. Among those who were STD-positive in the pre-linkage period, 91.7% and 77.8% of Hispanic and Black clients respectively, became STD-negative in the post-linkage period, compared to only 63.2% of White (non-Hispanic) clients doing the same. In other words, over a third of White clients who were infected with a STD in the pre-

linkage period continued their sexual behavior risks following linkage to care, higher than the overall prevalence of STDs in the post-linkage period. Further, over half of these clients (White non-Hispanic, STD infection in both pre and post-linkage periods) did not reach viral suppression during the year after HIV diagnosis/referral, highest percentage among any strata by ethnicity and pre/post-linkage STD status. However, this difference among ethnic groups was not observed in the pre/post-viral suppression comparison. As such, the persistence of high-risk sexual behaviors through HIV diagnosis and linkage may share similar root factors with the failure to achieve viral suppression (or lack of treatment adherence). Given that engagement in high risk sexual behaviors, concurrent STD infection with HIV, and unsuppressed viral load[27] all increase risk of HIV transmission, further research should be focused to identify factors related to this segment of the population.

This study provided a unique opportunity to compare the STD testing history of HIV-positive individuals at specific time frames before and after HIV diagnosis. STD infection was used as a proxy for high risk sexual behaviors due to the established associations between certain sexual behaviors and STD risk. A potential mechanism behind increased risky sexual behaviors, HAART complacency, has also been linked to increase STD incidence.[28] Further, in previous literature, STD infection has been used to validate other methods of assessing risky sexual behavior.[29,30] As such, it was reasonable to expect STD infection to represent sexual behaviors conducive to STD or HIV transmission to some degree. And although STD infections are not a perfect proxy for all risky sexual behaviors, the focus of this study was comparing the relative prevalence of high-risk sexual behaviors between groups or periods of time, rather than determining the absolute prevalence.

There are limitations in this study. First, due to the composition of the study population, results may not be generalizable to the general population near the AHF areas. The clients at AHF are approximately 90% men of which over 90% are known men who have sex with men (MSM). The limited sample size due to exclusion criteria also reduced power. Several of the observed measures of association were noticeably large in magnitude but were not statistically significant. As far as biases from exclusions, most of the clients in the linkage analyses had STD testing at AHF prior to HIV diagnosis. These clients, whether they were regular AHF wellness clients or used AHF services specifically for STD testing, may differ from individuals who did not regularly access healthcare services prior to HIV diagnosis. Further, analyses were limited to clients to who remained in the AHF system after linkage and viral suppression. If the clients who had left the AHF system differed from those in the analyses with regards to sexual behavior and STD testing, then a bias may exist. Another limitation is the use of a proxy method for assessing high risk sexual behavior. Although not subject to the recall and social acceptability biases that may be present in questionnaire methods[31], comparisons of sexual behavior based on STD testing may be biased if the reason and frequency of testing differs between comparison groups (or time periods in this scenario), and if not all STD tests were reflected in the data. As far as testing frequency, the mean number of STD tests per client were similar between the pre and post-periods in this study for both linkage and viral suppression groups. However, any STD testing performed outside the AHF system was not available for analyses and remains a potential source of bias.

Conclusion

Overall, high risk sexual behavior as reflected through STD infections was reduced following linkage and remained so through viral suppression due to the influence of possibly

HIV diagnosis and other unmentioned factors. Any potential HAART complacency effect on sexual behavior was not discernable in the results. However, a specific subgroup (STD-positive in both the pre and post-linkage period) was observed that did not appear to be influenced by these factors (HIV diagnosis, linkage, treatment adherence) in a similar manner as the overall study group. This subgroup of clients was also associated with a lower probability of timely viral suppression. Future research on the behavioral influence from various aspects of HIV should also focus on identifying these types of subgroups as they may diverge in their response to the same factors and thus, pose a higher risk to HIV/STD transmission. Further, the characteristics of these subgroups may not always be consistent with the risk profiles commonly observed for high risk sexual behaviors[32] or failure to reach viral suppression.[33,34] Targeted behavioral interventions[23] and sexual network analyses[35,36] together with identification of these subgroups would contribute to the HIV prevention and wellness efforts. More refined understanding in this area could be obtained in future research with larger study populations and more direct methods[37] of sexual behavior assessment.

TABLES

Table 4-1. Baseline Characteristics by Comparison Groups among HIV-positive clients at a national non-profit HIV care organization, 2012-2013

	Pre/Post Linkage	Pre/Post Initial Viral Suppression
Total	173	227
Male at birth	99.4	98.2
Mean age (standard dev.)	34.5 (10.0)	35.3 (10.4)
Age 35+	41.0	43.6
Race/ethnicity		
Black (non-Hispanic)	26.0	31.3
Hispanic	38.2	38.8
White (non-Hispanic)	31.7	27.7
Other	4.1	2.2
CD4 count < 200 copies/μL	12.7	13.2
Outreach/Partner Site	35.3	48.5
California Diag. Site	69.9	66.1
Presence of new STD infection		
Pre-period	32.4	21.6
Post-period	22.0	18.9

Table 4-2. STD Prevalence in Pre and Post Periods for Linkage and Viral Suppression among HIV-positive clients at a national non-profit HIV care organization, 2012-2013

	Post-Linkage				
Pre-Linkage	STD (+)	(%)	STD (-)	(%)	Total
STD (+)	11	19.6%	45	80.4%	56 (32.4%)
STD (-)	27	23.1%	90	76.9%	117 (67.6%)
Total	38	22.0%	135	78.0%	173

McNemar's test p-value = 0.03

	Post-VS				
Pre-VS	STD (+)	(%)	STD (-)	(%)	Total
STD (+)	10	20.4%	39	79.6%	49 (21.6%)
STD (-)	33	18.5%	145	81.5%	178 (78.4%)
Total	43	18.9%	184	81.1%	227

McNemar's test p-value = 0.48

Table 4-3. Associations with Sexual Behavior Change from Pre- to Post-Linkage among HIV-positive clients at a national non-profit HIV care organization, 2012-2013

	Overall		STD+ in pre-linkage period		Not STD+ in pre-linkage period	
	Univariate *p* value	Multivariate Odds Ratio (95% CI)	Univariate *p* value	Multivariate Odds Ratio (95% CI)	Univariate *p* value	Multivariate Odds Ratio (95% CI)
STD+ in pre-period	*<0.0001*	14.92 (6.41, 34.76)	--	--	--	--
Age 35+	*0.63*	0.71 (0.32, 1.58)	*0.21*	4.54 (0.76, 27.0)	*0.04*	0.36 (0.13, 1.03)
Race/ethnicity						
Black (non-Hispanic)	*0.10*	1.04 (0.36, 2.95)	*0.86*	3.14 (0.35, 28.0)	*0.51*	0.72 (0.21, 2.47)
Hispanic	*0.04*	1.94 (0.80, 4.75)	*0.07*	12.74 (1.61, 100.72)	*0.31*	1.11 (0.37, 3.34)
CD4 count < 200 copies/µL	*0.14*	0.71 (0.22, 2.29)	*0.78*	1.76 (0.10, 31.49)	*0.51*	0.72 (0.18, 2.89)
Site and Season of Diagnosis						
Outreach/Partner Site	*0.40*	1.74 (0.76, 3.97)	*0.23*	5.31 (0.73, 38.84)	*0.55*	1.54 (0.57, 4.17)
California	*0.83*	0.71 (0.30, 1.66)	*0.85*	0.65 (0.09, 4.70)	*0.56*	0.65 (0.24, 1.72)

Table 4-4. Associations with Sexual Behavior Change from Pre- to Post-Viral Suppression (VS) among HIV-positive clients at a national non-profit HIV care organization, 2012-2013

	Overall		STD+ in pre-VS period		Not STD+ in pre-VS period	
	Univariate *p* value	Multivariate Odds Ratio (95% CI)	Univariate *p* value	Multivariate Odds Ratio (95% CI)	Univariate *p* value	Multivariate Odds Ratio (95% CI)
STD+ in pre-period	*<0.0001*	16.80 (7.15, 39.48)	--	--	--	--
Age 35+	*0.33*	0.79 (0.39, 1.61)	*0.93*	1.16 (0.25, 5.44)	*0.48*	0.70 (0.31, 1.58)
Race/ethnicity						
Black (non-Hispanic)	*0.64*	0.95 (0.38, 2.35)	*0.97*	0.92 (0.12, 7.17)	*0.49*	0.97 (0.35, 2.75)
Hispanic	*0.79*	0.99 (0.43, 2.30)	*0.93*	0.76 (0.15, 3.84)	*0.75*	1.02 (0.37, 2.82)
CD4 count < 200 copies/µL	*0.03*	0.63 (0.19, 2.06)	*0.98*	--	*0.48*	0.84 (0.26, 2.71)
Site and Season of Diagnosis						
Outreach/Partner Site	*0.27*	1.03 (0.51, 2.10)	*0.18*	0.35 (0.08, 1.58)	*0.90*	1.40 (0.62, 3.18)
California	*0.44*	0.56 (0.26, 1.19)	*0.71*	0.89 (0.15, 5.41)	*0.05*	0.48 (0.20, 1.11)

CHAPTER 5

Conclusion

The overall study was able to identify the factors associated with progression to each stage of the HIV care continuum, determine the retention measure most effective as a prognostic tool by estimating the predictive accuracy, and evaluate potential change in sexual behavior along two significant events following knowledge of one's HIV infection. Aside from the immediate findings specific to our population, our study provided broader implications. In order to address factors that are observed to be associated with viral suppression, one cannot automatically assume that this association is persistent at every stage. Interventions need to be targeted to the specific stage of influence to be most effective. A gold standard retention measure may not exist. Therefore, ideally, retention measures should be evaluated against each other within any given population to determine the most appropriate measure. Statistical learning techniques can be valuable for this process.[38] From the behavioral perspective, evaluation of factors influencing sexual behavior change at linkage or viral suppression may also aid in identification of subgroups at high-risk for further transmission. Consideration of these issues may help in program planning and evaluation.

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