

Identifying Factors Related to Unsuppressed Viral Load among Older People Living with HIV

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AMIDA CARE–BROOKDALE RESEARCH COLLABORATIVE

Mission

The mission of the Amida Care/Brookdale Research Collaborative (ABRC) is to develop and conduct high-quality, safe, and effective research involving Amida Care members, providers, and the community. The multidisciplinary research agenda of the ABRC is driven by needs identified by a variety of participants, including academic researchers, network providers, Amida Care members, pharmaceutical companies, and leaders in the public health, managed care, and policy sectors.

Vision

The ABRC comprises a research infrastructure that enables a range of research efforts such as:

- Epidemiological studies
- Psychosocial and behavioral research
- Clinical and pharmacologic studies and trials
- Applied and translational research
- Outcomes research
- Evaluation studies

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BACKGROUND

In 2015, New York State launched its “Ending the Epidemic” (ETE) Blueprint (New York State Department of Health, 2015), an initiative to end AIDS that has gained traction with similar efforts across the U.S. and internationally (Stover et al., 2016). One of the three ETE goals is aimed at people who are diagnosed with HIV: “...to link and retain persons diagnosed with HIV to health care and get them on anti-HIV therapy to maximize virus suppression so they remain healthy and prevent further transmission.” The purpose of our study was to identify factors associated with unsuppressed HIV viral load in older and younger adults, and to understand how these factors may differ between those ages 50 and older and 49 and younger. People with HIV (PWH) engaged in care and virally suppressed can achieve life expectancies similar to non-infected peers (Samji et al., 2013). As a result, people 50 and older are now estimated to constitute the majority of PWH in the U.S. (High et al., 2012) and in other nations where access to anti-retroviral therapy (ARV) is widely available (Mahy et al., 2014). To date, we have little information concerning how the challenges of aging with HIV might affect achieving and maintaining viral suppression among adults 50 and older.

To implement programs that address the three goals of the ETE Blueprint, in 2016 the New York State Department of Health AIDS Institute initiated collaborations with managed care organizations with Special Needs Plans for PWH who are Medicaid recipients. To this end, the New York State Department of Health provides an annual report to the managed care organizations of plan members who have an unsuppressed HIV viral load, or no viral load reported. The identification of these members, called ETE cohorts, has occurred since 2016. One of the managed care organizations involved in this effort is Amida Care, a Medicaid Special Needs Plan for PWH or those at risk for HIV infection in New York City with over 7,500 members with HIV. Forty-eight percent of the Amida Care ETE cohort was age 50 or older in 2016. Preliminary analyses of the first 2016 ETE cohort indicated that lack of a stable connection to a pharmacy and poorly managed behavioral health issues contributed to the failure of achieving viral suppression among ETE cohort members (Tocco et al., 2017).

While these preliminary analyses have been an important first step, much remains to be learned about what distinguishes PWH who are able to achieve viral suppression from those who remain unsuppressed or those who are unable to maintain viral suppression. We also have little understanding of how complications due to aging with HIV, such as increased multimorbidity and polypharmacy issues and long-term survival, might play a role in achieving viral suppression among PWH. The availability of detailed health and healthcare utilization data over four years from the Amida Care ETE cohorts, along with a comparison group who have been consistently virally suppressed, provides a unique opportunity to answer these questions and provide the evidence base to more effectively tailor programs and interventions to assist older PWH in achieving and maintaining viral suppression.

OBJECTIVES AND METHODS

The purpose of this study was to identify factors associated with unsuppressed HIV viral load in PWH, and to understand how aging and age-related factors (multimorbidity, polypharmacy) are associated with viral suppression.

This study involves a retrospective chart review and data analysis of the 3,265 members of the Amida Care managed care plan who were continuously enrolled from 2016 through 2019 who were HIV positive and 18 years or older. We examined independent factors that differentiate five viral suppression groups: PWH who were consistently unsuppressed, PWH who became unsuppressed, PWH whose suppression fluctuated, PWH who achieved sustained viral suppression, and PWH who were consistently virally suppressed. We used cluster analysis to classify viral suppression patterns among Amida Care members. The study protocol was approved by the City University of New York Institutional Review Board.

We obtained the following variables in seven domains to perform the analyses: 1) demographics (age group, race/ethnicity, gender identity); 2) physical health (ICD-10 diagnosis codes, actuarial risk scores, comorbid conditions, CD4 t-cell count, number of comorbid conditions); 3) behavioral health (depression, anxiety, bipolar, schizophrenia, post-traumatic stress disorder [PTSD], alcohol, tobacco, drug use, opioid use disorder, number of behavioral health conditions); 4) health care utilization (number of: inpatient hospital visits, outpatient hospital visits, emergency room visits, primary care visits, behavioral visits, and costs [total, pharmacy, medical]); 5) pharmacy utilization (type of prescription, ARV fills, antidepressive medication fills, other psychotropic medication fills, all other medication fills, number of pharmacies used, total costs); 6) proportion of days covered (PDC) medication adherence¹ [HIV, other medications]; 7) program participation (Health Home, Adult Day Health Care [ADHC], Health and Recovery Plan for substance use [HARP], homeless services).

In terms of specific aging concerns in these variable domains, we assessed the impact of multimorbidity through physical health measures (diagnosis codes, actuarial risk scores, number of comorbidities), behavioral health categories, and health care utilization measures. Polypharmacy was determined by the number of types of medication fills (i.e., five or more medications). Reconstitution of the immune system was assessed by CD4 t-cell counts.

Hypothesis 1: The lack of a stable connection to a pharmacy (i.e., using more than one pharmacy) and poorly managed behavioral health issues contribute to the failure of achieving viral suppression. We performed bivariate zero-order correlational analysis between viral suppression groups and independent variables to better understand the pattern of relationships between viral suppression patterns and independent variable domains. We then performed multinomial logistic regression analyses by variable domain and tested an aggregate model of independent variables significantly related to suppression patterns across domains.

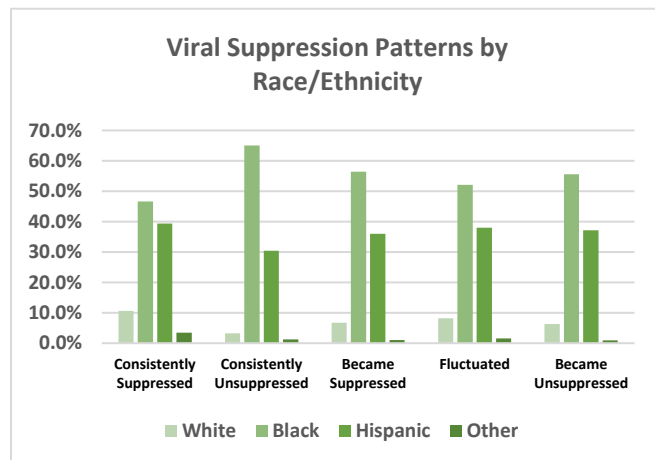
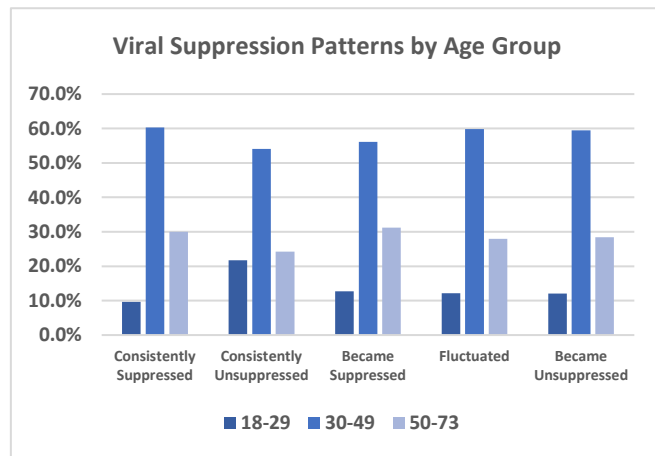
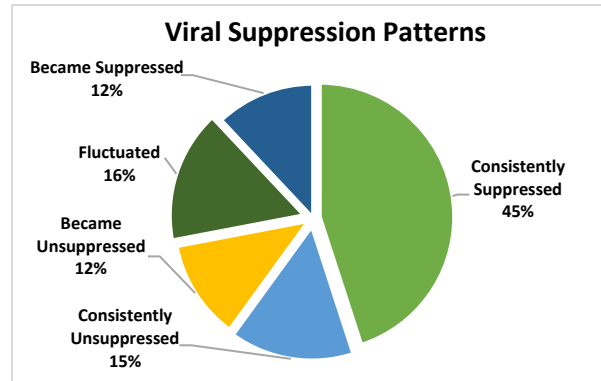
Hypothesis 2: Age-related factors may affect viral suppression. To examine the impact of age-related factors to viral suppression status, we used multinomial logistic regressions. Specifically, we examined the association of age, as well as the number of physical and behavioral health conditions (multimorbidity) and polypharmacy (five or more medications), as these two factors increase as PWH age (High et al., 2012), with consistent viral suppression, intermittent suppression, and consistent non-suppression.

FINDINGS

Of the 3,265 HIV-positive Amida Care members in the data set, viral suppression information for 2,677 was sufficient to classify them into one of the five groups for the period 2016-2019: consistently

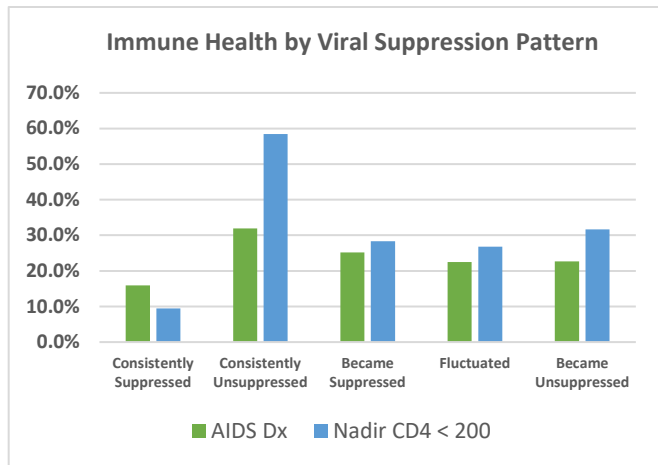
¹ The PDC is calculated by the ratio of the number of days the patient is covered by the medication to the number of days the patient is eligible to have the medication on hand.

unsuppressed (n = 401), became unsuppressed (n = 331), suppression fluctuated (n = 426), became suppressed (n = 314), and consistently suppressed (n = 1,205).² Bivariate analysis found significant associations with viral suppression group in the domains of demographics, physical health, behavioral health, health care utilization, pharmacy utilization, treatment adherence, costs, and program participation.



Demographic Characteristics. Regarding demographic factors, PWH who were 18 to 29 years of age were less likely to be consistently suppressed and more likely to be consistently unsuppressed. Those who were 30 to 49 years and 50 years and older were more likely to be consistently suppressed or to become suppressed over the study period. PWH who were non-Hispanic Black, who made up 53% of the sample, were under-represented in the consistently suppressed group (47%) and over-represented in the consistently unsuppressed group (65%). Non-Hispanic Whites and Hispanics showed the opposite pattern and had a greater likelihood of being consistently suppressed than consistently unsuppressed. There were no clear patterns by race/ethnicity in the intermittent suppression groups (became suppressed, fluctuated, became unsuppressed). In terms of gender identity, PWH who were transgender or gender diverse had a greater likelihood of

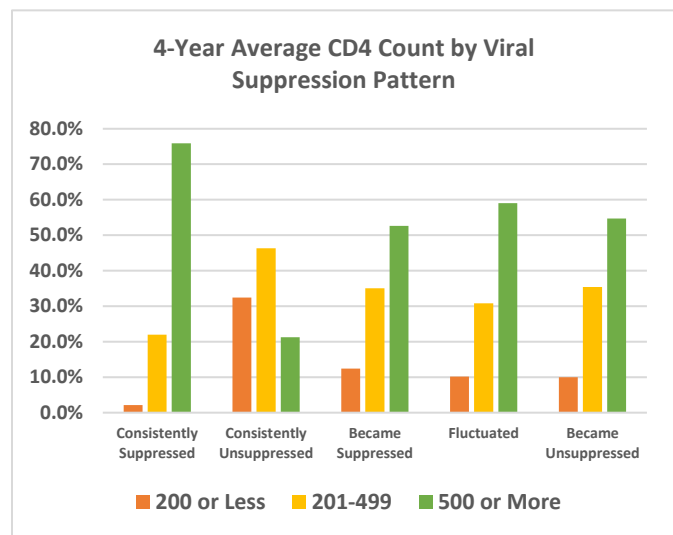
² To determine viral suppression patterns, members needed to have viral load information for three of the four years of the study. Viral suppression was defined as undetectable HIV viral load. Members were classified as unsuppressed in a year if they had detectable HIV viral loads at any point during that year.



being in the fluctuating viral load group. There did not appear to be an association of being cisgender (female or male) with viral suppression patterns.

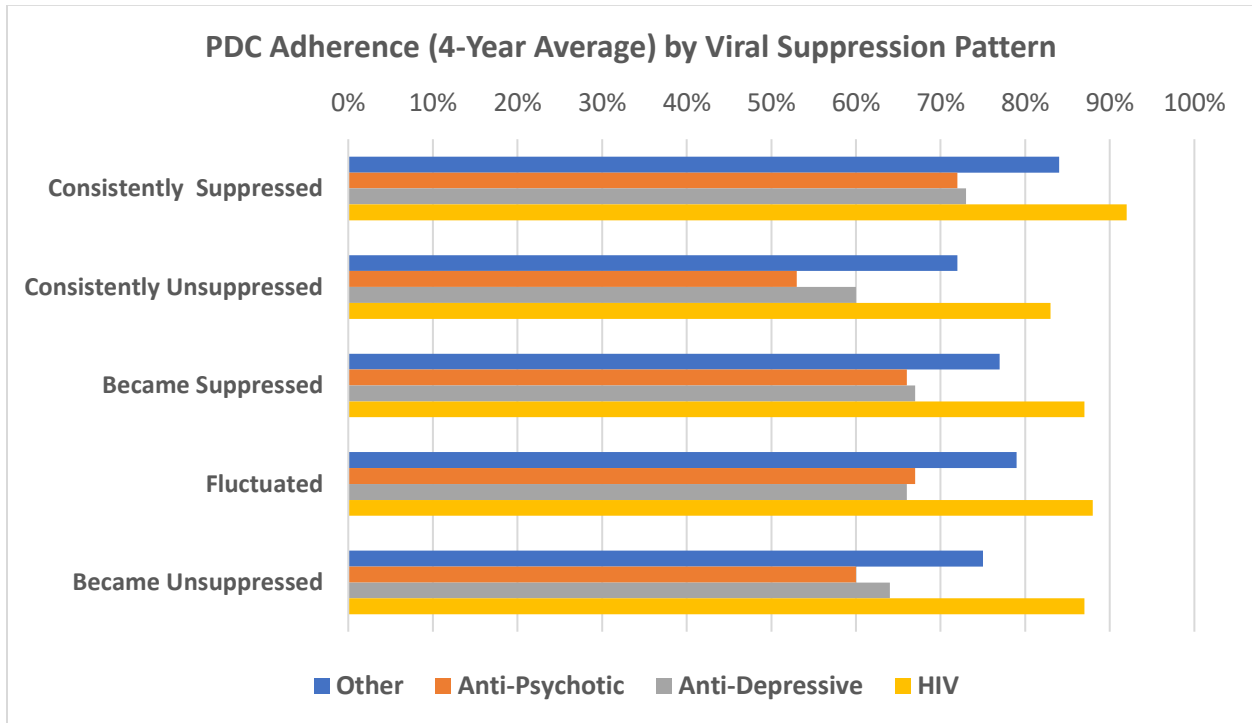
Immune Health. Both prior and current indicators of immune system health during the four-year study period were related to viral suppression patterns. PWH who had received a diagnosis of AIDS were significantly more likely to be consistently unsuppressed or in one of the intermittent viral suppression groups, and less likely to be consistently suppressed compared to those not

diagnosed with AIDS. In addition, having experienced a severe impairment of the immune system (i.e., CD4 t-cell count nadir of 200 or less) was strongly associated with being consistently unsuppressed or intermittently suppressed. Current CD4 counts were not surprisingly strongly related to viral suppression pattern, with those being consistently suppressed the most likely to have a CD4 count of 500 or greater. Looking at average CD4 counts over the four years of the study, approximately 80% of those who were consistently suppressed had CD4 counts of 500 or more; nearly four times the rate of the consistently unsuppressed group (21%). This compares to approximately 50-60% of PWH in the intermittent suppression groups who had CD4 counts of 500 or more. Approximately 10% of these PWH who were intermittently suppressed had CD4 counts of 200 or less compared to 30% of those who were consistently unsuppressed.



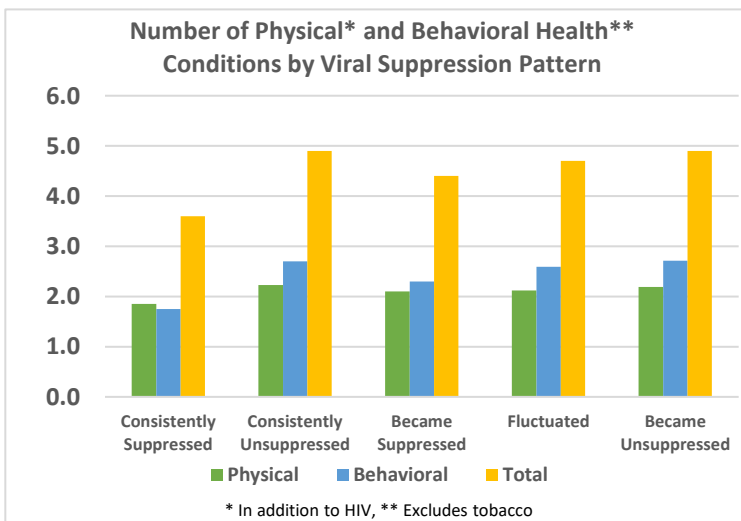
Medication Use and Adherence. Pharmacy use varied by type of medication. The consistently unsuppressed group had the highest use of antidepressants and antipsychotics as well as higher use of LABA/LAMA for COPD, but much lower use of statins and cholesterol/lipid medication and lower use of diabetes medication (not insulin). The consistently unsuppressed, became unsuppressed, and fluctuating groups used greater numbers of pharmacies on average (1.8, 1.6, and 1.6, respectively) compared to the consistently suppressed and became suppressed groups (1.4 and 1.5, respectively). On average, PWH in this sample were using five prescribed medications and the proportion of polypharmacy did not differ by viral suppression pattern.

Adherence to any type of medication was generally highest for the consistently suppressed and lowest for the consistently unsuppressed, with the intermittent suppression groups falling in between. However, adherence to HIV medications was better than adherence to any other class of medication for all viral suppression groups.



Physical and Behavioral Health.

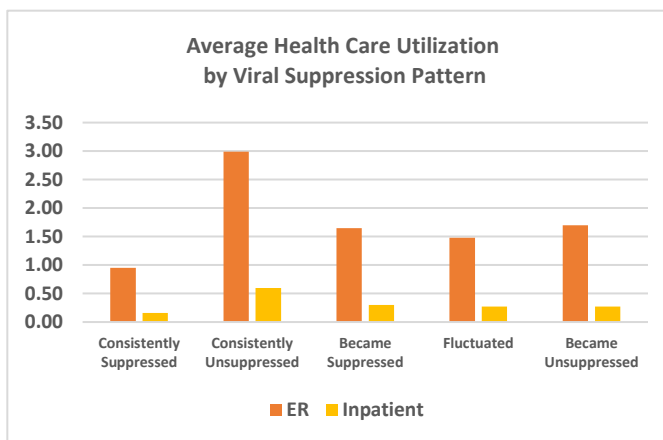
Those who were consistently unsuppressed were more likely to have diagnoses of asthma, COPD, and hypertension, and less likely to have a diagnosis of diabetes. Hepatitis C and diabetes had the highest prevalence in intermittently suppressed groups. Depression, bipolar disorder, schizophrenia, and PTSD were associated with a lack of suppression. Anxiety, however, was notably lower in the consistently unsuppressed group than in the consistently suppressed group. Drug and alcohol use claims were notably higher among in the intermittently suppressed groups and especially the consistently unsuppressed group.



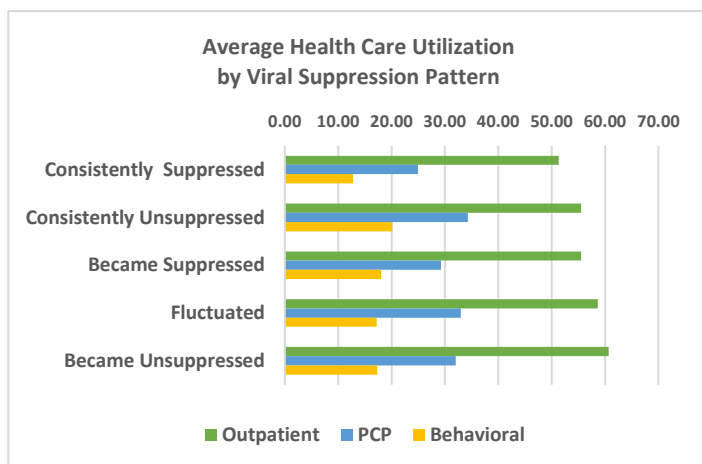
In terms of multimorbidity, sustained viral suppression showed a linear association with the number of physical health conditions (excluding HIV) and behavioral health conditions (excluding tobacco-smoking cessation).³ PWH who were consistently unsuppressed or became unsuppressed had the highest average number of physical health conditions (2.2), followed by those who became suppressed or fluctuated (2.1) and PWH who were consistently suppressed (1.9). The average number of behavioral health conditions followed the same pattern, but the differences were more pronounced. PWH who were consistently unsuppressed or became unsuppressed had the highest average number of behavioral health conditions (2.7), followed by those who fluctuated (2.6) or became suppressed (2.3) and PWH who were consistently suppressed (1.8). In terms of combined multimorbidity (physical + behavioral conditions), the consistently unsuppressed and became unsuppressed groups had 4.9 conditions on average, as compared with 4.7 conditions for the fluctuating group, 4.4 for the group that became suppressed, and 3.6 for the consistently suppressed group.

Health Care Utilization and Cost.

Health care utilization data paralleled findings on differences in multimorbidity by viral suppression pattern. PWH who were consistently unsuppressed were the most likely to use the emergency room (ER). Looking at annual utilization over the four



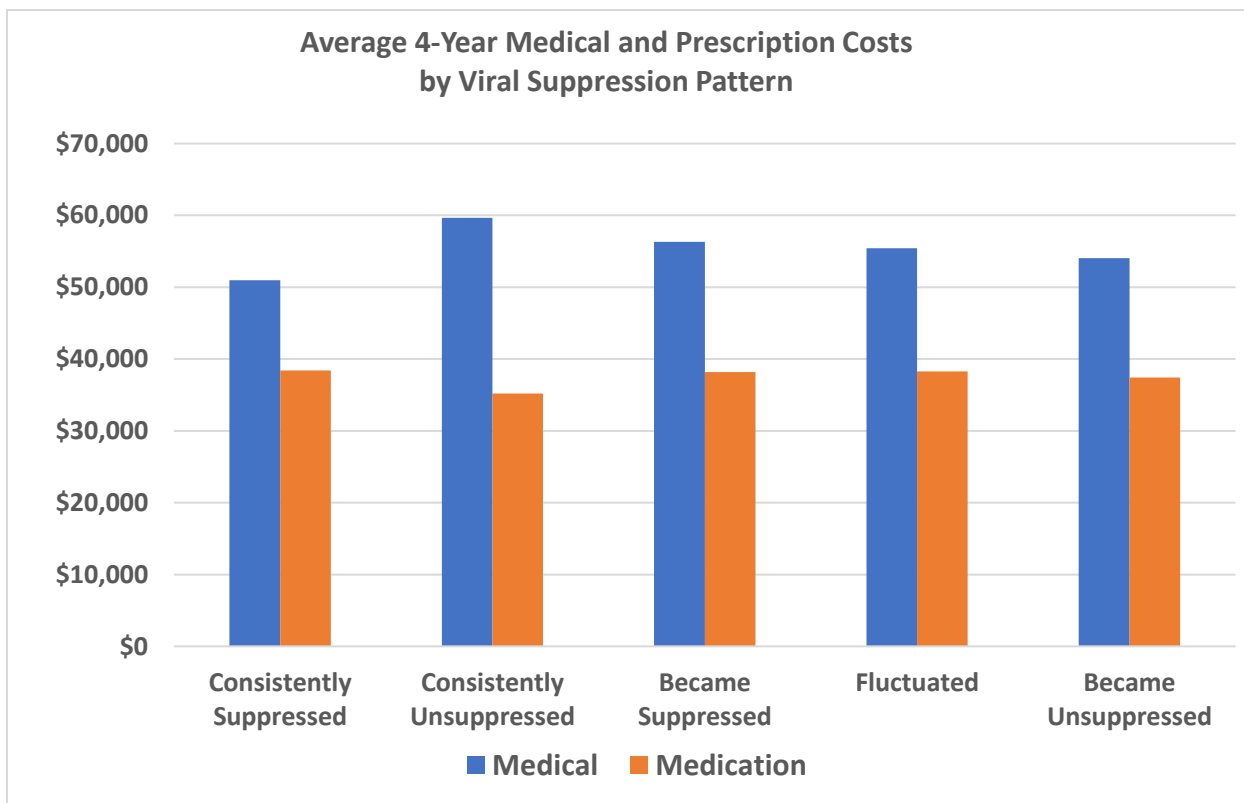
years of the study, those who were consistently unsuppressed had an average of 3 ER visits, compared to approximately 1 visit for the consistently suppressed. Those who were in the intermittently suppressed groups were in between with an average of 1.5 ER visits per year. Consistently unsuppressed PWH also had the highest average level of inpatient hospital stays per year (0.6), as compared with approximately 0.3 on average for the intermittently suppressed groups and 0.2 stays for the consistently suppressed group.



The consistently suppressed group had the lowest number of behavioral health, primary care physician (PCP), and outpatient hospital claims compared to PWH who were intermittently or consistently unsuppressed. PWH who were consistently unsuppressed had the

³ Physical and behavioral health condition diagnoses were obtained from inpatient hospital claims and from opioid treatment data over the four years of the study.

greatest annual average number of behavioral health and PCP claims, while PWH who became unsuppressed had the greatest number of outpatient claims. Consistent with findings on behavioral health conditions, HARP and Adult Day Health Care eligibility were significantly associated with lack of viral suppression. Homelessness was substantially overrepresented among the consistently unsuppressed, emphasizing the importance of securing stable housing for PWH in order to meet viral suppression targets. Overall, the consistently suppressed had the lowest medical costs and the consistently unsuppressed had the lowest prescription costs. Combined medical and prescription costs over four years did not show significant differences between groups, but combined costs were highest for the group that became suppressed in 2017, and for the consistently unsuppressed group in 2019.



Multivariable Analysis. We then performed multinomial logistic regressions for all variable domains and created a final model with the most significant factors across all domains. The findings from this model show the factors with the strongest associations with viral suppression group, holding the other factors constant (Table 1). For example, members who have had a nadir CD4 count below 200 have nine times the odds of being in the consistently unsuppressed group rather than the consistently suppressed group, and more than twice the odds of being in one of the intermittently suppressed groups. Members who used drugs had around twice the odds of being intermittently or consistently unsuppressed. Members with antipsychotic prescriptions had 1.7 greater odds of being consistently unsuppressed than consistently suppressed. In terms of demographics, members at least 30 years old had two-thirds lower odds of being consistently unsuppressed than 18- to 29-year-olds. Non-Hispanic Blacks had five times the odds of being in the consistently unsuppressed group compared with non-Hispanic Whites. Gender identity was not related to viral suppression patterns in this analysis when controlling for other factors.

Table 1. Multinomial Logistic Regression of Viral Suppression Patterns, Final Model Across Domains

Factors	Became Suppressed		Fluctuated		Became Unsuppressed		Consistently Unsuppressed	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
CD4 ever below 200	2.372***	1.554–3.621	2.794***	1.925–4.054	3.841***	2.606–5.661	9.056***	6.159–13.317
Drug use	1.904**	1.305–2.779	1.943***	1.397–2.703	2.559***	1.750–3.741	2.352***	1.568–3.528
Sum of ER visits	1.022*	1.004–1.041	1.009	.989–1.028	1.014	.995–1.034	1.027**	1.009–1.045
Antipsychotic Rx	1.585*	1.080–2.328	1.393	.994–1.952	1.564*	1.082–2.260	1.724**	1.174–2.532
MMTP participation	.843	.546–1.302	1.176	.814–1.700	1.129	.755–1.690	1.306	.856–1.993
# pharmacies used	1.086	.861–1.371	1.259*	1.034–1.532	1.229	.994–1.518	1.443**	1.172–1.777
HIV adherence	.091**	.021–.390	.209*	.051–.862	.118**	.028–.494	.065***	.015–.274
Other med adherence	.221**	.075–.646	.434	.163–1.152	.122***	.045–.333	.116***	.041–.328
# years HARP eligible	1.017	.918–1.126	1.005	.919–1.099	.998	.904–1.103	.996	.896–1.107
Eligible for ADHC	1.119	.625–2.005	1.964**	1.254–3.078	2.397***	1.492–3.850	1.924*	1.150–3.217
Demographics:								
Age 18-29	Ref.							
Age 30-49	1.248	.479–3.251	.699	.367–1.657	.819	.359–1.865	.341**	.167–.697
Ages 50 and Older	1.394	.523–3.715	.780	.320–1.525	.787	.335–1.848	.326**	.153–.695
White non-Hispanic								
White non-Hispanic	Ref.							
Black non-Hispanic	2.127	.996–4.542	1.331	.743–2.383	1.407	.723–2.738	5.098**	1.724–15.075
Hispanic	1.778	.829–3.817	1.117	.621–2.011	1.145	.585–2.241	2.874	.962–8.588
Other non-Hispanic	.382	.045–3.265	.858	.273–2.692	.454	.090–2.300	1.609	.247–10.494
Male cisgender								
Male cisgender	Ref.							
Female cisgender	.922	.651–1.304	.988	.724–1.348	.903	.642–1.271	.881	.615–1.263
Transgender	.555	.206–1.496	1.609	.859–3.014	.766	.329–1.785	1.357	.634–2.905
Notes: MMTP = Methadone Maintenance Treatment Program; HARP = Health and Recovery Plan; ADHC = Adult Day Health Care. N = 1,687 (Consistently Suppressed [reference group], N = 782; Became Suppressed, N = 187; Fluctuated, N = 267; Became Unsuppressed, N = 216; Consistently Unsuppressed, N = 235). Cox and Snell pseudo $R^2 = .273$. *** $p < .001$; ** $p < .01$; * $p < .05$.								

CONCLUSIONS

Our examination of viral suppression patterns in a sample of PWH enrolled in a Medicaid managed care plan found that approximately one-half (45%) were able to achieve sustained viral suppression over a four-year period, while 15% were consistently unsuppressed. The remaining 40% showed intermittent patterns of viral suppression, either transitioning to suppressed or unsuppressed status, or fluctuating between suppressed and unsuppressed states. Looking at our findings overall, these PWH with intermittent suppression present the same profile regardless of subgroup classification. It is possible that within the intermittent group those classified as becoming suppressed or becoming unsuppressed are not distinguishable from those in the fluctuating group. Thus, our observations and classification in the current study may represent a compressed snapshot of what is, in fact, three sub-populations that fluctuate between suppressed and unsuppressed status.

While demographic factors of age, race/ethnicity, and gender identity tended to be minimized in the final multivariate analysis, they were prominent in the bivariate analysis and in the multivariate analysis by domain, which are not presented in detail in this report. From a practical standpoint, demographic information is useful in identifying groups at risk for unsustained viral suppression, namely young adults from 18 to 29 years of age, people who are non-Hispanic Black, and those who identify as transgender or gender diverse. These findings are consistent with other research on social determinants of health among PWH, and future research should examine how to reduce barriers to accessing healthcare and medications for these groups (Bukowski et al., 2018; Chakraborty et al., 2015; Crepaz et al., 2017).

Our first hypothesis, that PWH with an unstable connection to a pharmacy and those with behavioral health problems would be at greater risk for being intermittently or consistently unsuppressed, was supported. In bivariate analysis, a number of behavioral health diagnoses (depression, bipolar, schizophrenia, drug use) were associated with having unsuppressed viral loads. This association was also apparent in our multivariable analysis, where both a greater number of pharmacies used and behavioral health indicators (drug use, antipsychotic medications, ADHC participation) were associated with greater odds of not being virally suppressed.

Our second hypothesis about the association of age and age-related factors of multimorbidity and polypharmacy to viral suppression patterns was partially supported. We found that PWH who were older had a greater likelihood of being virally suppressed. Polypharmacy did not emerge as a significant factor, which may be due in part to the high average number of prescribed medications across the viral suppression groups. However, physical and behavioral health multimorbidity was strongly associated with viral suppression patterns in a nearly linear fashion, with greater multimorbidity evident in the consistently unsuppressed group and among PWH who transitioned to an unsuppressed state. This translated into higher medical costs for these groups as well.

IMPLICATIONS FOR ETE PROGRAMMING

Given the strong associations between viremia and physical and behavioral health multimorbidity, it appears that failure to maintain durable viral suppression is part of a syndrome of poor health in this population of PWH. While viremia has been shown to lead to poorer clinical outcomes among PWH (Ghidei et al., 2013), it also appears that severe damage to the immune system as evidenced by a past diagnosis of AIDS and/or a nadir CD4 count of less than 200 may have lasting effects on PWH health and well-being across the lifespan. While continued efforts to achieve viral suppression among PWH are

critical, it is equally important that we attend to their other medical conditions at the same time. As noted in the Ending the Epidemic Advisory Group Report on implementation strategies for older adults in New York State (Luniewicz et al., 2016), it is essential to address the diagnosis and ongoing care of comorbidities that become more common as PWH age if the ETE effort is to be successful. This may require making more resources available to improve access and intensity of patient care.

Next, our findings make clear that New York State ETE will not be able to achieve its targets of community viral suppression levels without a substantial investment in increased and more effective behavioral health care for PWH. We must find ways to increase the capacity of our health care system to address these behavioral health needs. All too often, treatment for these conditions consists of prescription medication with periodic visits for medication management. However, it is well-known that medications for behavioral health problems are most effective when coupled with some type of adjunct therapy (e.g., individual counseling, group therapy) (Brennan-Ing et al., 2017; Brennan et al., 2005). In addition, better information on the effectiveness of behavioral health interventions among PWH with complex needs is critical for developing programs to improve viral suppression for this subpopulation.

While the identification of ETE cohorts as targets for specialized programs to improve adherence has been successful, it is clear that for PWH who are consistently unsuppressed this level of intervention has not been sufficient and greater programmatic support is warranted. Furthermore, PWH who are intermittently suppressed or continuously unsuppressed present with myriad inter-related risk factors for non-suppression (e.g., mental illness and unstable housing), requiring individually tailored care plans for viral suppression interventions and perhaps a modification of health care delivery systems to be successful. Milestones toward achievement of viral suppression should be articulated for these patients and the success of the care plan can be assessed in terms of the achievement of these milestones. We must also realistically recognize that for some PWH, sustained viral suppression may be an unachievable goal; however, our current study shows that even intermittent suppression is associated with better health, albeit not as good as for the consistently suppressed. Thus, intermittent suppression could be an important milestone for PWH who are consistently unsuppressed.

Utilization of our findings has the potential to increase the health-related quality of life for both older and younger PWH by improving health care delivery and clinical outcomes and informing the development and refinement of models of care. Further, helping older PWH maintain viral suppression has the potential to constrain costs over the long term and reduce HIV incidence by preventing transmission of the virus to others.

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