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Association of ART regimen and adherence to viral suppression: an observational study of a clinical population of people with HIV

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Abstract

Adherence to antiretroviral therapy (ART) is essential for the effective management of HIV, which includes keeping the HIV viral load undetectable. This study aimed to determine whether certain ART medications are more "forgiving" of poor adherence in achieving viral suppression. We identified subgroups of ART medication usage and determined the extent to which ART adherence is associated with viral suppression across those subgroups. Data came from claims and clinical records (2017–2019) of 3,552 HIV-positive adult members of a Medicaid managed care plan. Pharmacy fill data were examined to characterize ART medications using latent class analysis (LCA), which captures the complexity of real-world ART usage (i.e., multiple medications, ART switching). LCA yielded five ART medication patterns over three years, mostly characterized by recent medications and formulations of ART, though they varied in number of tablets and in medication class. Mixed effects logistic regression models were estimated to determine whether odds of viral suppression differed by ART adherence level. After adjusting for covariates, those with at least 90% adherence (i.e., 90 to < 95%) did not significantly differ from those with 95% adherence or greater in terms of viral suppression, which corroborates existing clinical recommendations. These findings can inform provider-patient communication for people with HIV, especially those who have difficulty maintaining adherence. This includes those experiencing unstable housing, mental health conditions, or substance use.

Keywords HIV/AIDS, Antiretroviral therapy, ART, ART adherence, Viral suppression, ART forgiveness

Suboptimal viral suppression over time is associated with poorer clinical outcomes [1]. Further, virological suppression is the cornerstone of "treatment as prevention," since people with HIV (PWH) with undetectable HIV RNA (<200 copies/mL) cannot transmit HIV through sexual contact [2, 3]. Most ART regimens that are used today are more "forgiving" of poor adherence and allow people with HIV (PWH) to be virally suppressed at lower adherence levels than previously recommended (i.e., <90–95%) [4, 5]. ART forgiveness means maintaining virological suppression and avoiding resistance despite suboptimal adherence. In this study we examined two critical factors—ART medication and adherence—to determine whether certain ART types (i.e., medications or medication classes) are more "forgiving" of poor adherence in achieving viral suppression.

Achieving and maintaining virological suppression among PWH is multifactorial and influenced by ART

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regimen type, adherence, and patient factors [6]. Different ART formulations, composed of distinct drug classes, have variable thresholds for treatment failure and the development of resistance [7]. Importantly, among contemporary ART regimens, such as those that are non-nucleoside reverse-transcriptase inhibitor-based (NNRTIs), virological suppression has been observed at adherence levels between 54% and 100% [7, 8]. Similar recent work has observed differences in the association between regimen type and forgiveness among ART regimens that include integrase strand transfer inhibitors (INSTIs) [9]. For example, bictegravir- and dolutegravir-based therapies have higher resistance barriers compared with the earlier INSTIs, elvitegravir and raltegravir [10]. Using data from the Veterans Health Administration, one study found that regardless of ART regimen, patients with adherence levels of at least 75% did not differ from those with over 95% adherence in terms of viral suppression [11]. It is notable, however, that the majority of recent empirical work examining ART forgiveness has been conducted in closely controlled clinical trials that assess a limited number of ART regimens or similar intervention or evaluation studies [12], and are not representative of real-world patients or situations.

Understanding ART forgiveness beyond the context of tightly controlled clinical studies is critical for improving rates of virological suppression in populations of PWH with medication adherence challenges. For example, behavioral health conditions, such as depression and substance use disorder, may impede ART adherence [13–18]. PWH with unstable housing may be at risk for ART non-adherence due to competing survival demands and difficulty with access to and engagement in care [19, 20]. Finally, transgender and gender-diverse PWH experience higher rates of both behavioral health challenges and housing instability, which also affects adherence and leads to lower rates of viral suppression compared to cisgender peers [21, 22].

The Ending the HIV Epidemic in the United States initiative aims to increase viral suppression among PWH to 95% by 2025, and efforts are still underway to reach this goal [23]. Patient-based research in real-world settings that may contribute to meeting the goals of this initiative is lacking. Most studies that focus on adherence and forgiveness compare a limited number of specific regimens, which may not reflect ART utilization patterns in the general population. Given the myriad of new ART formulations available, our primary objectives were to identify patterns of medication usage using multi-year data from a real-world clinical population and determine the extent to which these medications were more forgiving of poor adherence. We also examined the association of risk factors for non-adherence, including behavioral health conditions, unstable housing, and transgender and gender-diverse identities in relation to ART forgiveness.

Method

Participants

Data were obtained from the claims and clinical records of members of Amida Care, a Medicaid managed care plan in New York City, who were living with HIV, 18 years or older, and continuously enrolled in the health plan from 2017 to 2019. Our analytic sample included those with valid pharmacy data ($n=3,552$).

Measures

ART medication

Due to various, irregular ART medication fill dates, we examined medications by calendar quarters. There were 46 individual medications and over 1100 unique combinations across the 12 quarters in the study period. After excluding medications with very low frequencies (<1% of fills each year), there were 21 medications represented in 2017, 24 in 2018, and 24 in 2019. Excluding uncommon medications did not reduce the sample size.

Adherence to ART medication

The proportion of days covered (PDC) was used to assess adherence, based on pharmacy claims data to reflect the proportion of days a person has medication available from filled prescriptions during the year [24]. Adherence categories included: 1)<50%; 2) 50–80%; 3)>80–90%; 4)>90–95%; 5)>95%.

HIV viral suppression

The primary outcome, viral suppression, was defined by HIV RNA (viral load) of <200 copies/mL, in line with well-established standards and to account for variation in the sensitivity of tests used by multiple labs [25]. Participants had 0 to 20 viral load tests recorded per calendar year. If a participant's tests included at least one unsuppressed result, they were considered unsuppressed for that year.

Covariates

We included covariates based on past empirical findings. Nadir CD4 T-cell count was dichotomized (1=greater than or equal to 200 cells/μL, 0=less than 200 cells/μL). Physical comorbidities and behavioral conditions were based on diagnosis codes and comorbid conditions available in the data in the past year. Quarters that included a regimen switch (i.e., medications filled that quarter were different from the previous quarter) were summed for each year. Age (18–29, 30–49, 50+), race/ethnicity (non-Hispanic Black, Hispanic, non-Hispanic White, and non-Hispanic other race), and gender identity (cisgender male, cisgender female, transgender/gender diverse) were

categorical variables. Housing status denoted members who met criteria for a program for those with unstable housing.

Analytic Strategy

Identification of patterns of ART medication

Due to the high number of individual ART medications and medication combinations represented within each quarter, we used latent class analysis (LCA) as a data reduction technique to categorize ART medication use by members. LCA is a statistical method used to identify patterns in data by grouping individuals into discrete, mutually exclusive latent classes (i.e., patterns) based on responses to indicator variables [26]. The present study used 24 individual ART medications as indicator variables. The goal is that individuals with similar patterns of ART medication usage will be grouped together, resulting in fewer patterns than if we were to analyze individual regimens. These patterns may indicate, for example, medications that are commonly prescribed together, medications associated with regimen switches, etc. LCA has previously been used to cluster individuals' prescription drug use, particularly for medically complex conditions or among individuals with multiple comorbidities [27, 28]. We used members' last valid quarter from each year to indicate whether each medication was filled [1] or not (0) for simplicity, given that most members' regimens remained consistent across quarters each year. This person-centered approach captures some complexity of real-world ART usage, including multiple medications and ART switching.

We tested two- through seven-class LCA models in MPlus Version 7.4 [29]. We determined the appropriate number of profiles using Bayesian information criterion, Lo-Mendell-Rubin tests, and entropy, as well as interpretability and meaningfulness (e.g., whether latent classes are distinct, easy to label, and logical) [30]. Posterior profile membership probabilities were used to assign respondents to a profile in the best fitting model.

ART medication patterns and viral suppression

First, logistic regression models were estimated for each latent class individually to determine whether odds of viral suppression differed by ART adherence level. Next, to address the nonindependence of our observations due to repeated measures, we estimated a series of mixed-effects logistic regression models. The two-level models included random effects for the participant level, which accounted for the clustering of three time points (level 1) within participants (level 2). Including participant as a random effect allowed us to model within-participant variance and account for this shared error [31]. The fixed effects included the main independent variables, latent class and adherence, as well as covariates (nadir CD4, counts of physical comorbidities and behavioral conditions, regimen switch quarters per year, quarters that involved a regimen switch, age category, race/ethnicity, gender identity, and unstable housing).

We compared participants who had complete viral load data (i.e., not missing in any year, $n=2{,}770$) to those who were missing viral load data for one or more years ($n=783$) on key demographic and health characteristics using t-tests and chi-square tests. Those with missing data had a lower proportion with a nadir CD4 below 200 (17.9% versus 24.7%; X^2 (1) $=15.94$, $p<0.001$) and had fewer behavioral conditions (M = 1.81 versus 2.27; $t(3550)=6.08$, $p<0.001$). All statistical analyses were performed using RStudio, version 7.1 [32, 33].

Results

Demographics

Of the analytic sample ($n=3{,}552$), 63% identified as cisgender men, 54% were non-Hispanic Black, and 57% were aged 30 to 49 (Table 1). About two-thirds of the sample were at least 90% adherent to ART each year, and 55.5–58.4% of the entire sample had an undetectable viral load.

Patterns of ART medication

The best fitting model yielded six unique ART medication patterns over three years, each characterized by different medications (Table 2). The medications that were most divergent among the latent classes were used to characterize and name them. As a result, these latent classes, or patterns, do not necessarily represent ART regimens. Three patterns were consistently identified each year, two patterns were identified in 2018 and 2019, and one pattern was identified in 2017 only. We detail each below:

LCA 1 was characterized by three medications: dolutegravir (DTG), emtricitabine/tenofovir alafenamide (FTC/TAF), and darunavir/cobicistat (DRV/COBI). The drug classes represented by these medications are INSTI, combination NRTIs, and boosted PI. This pattern made up 26% of the sample in 2017, 25% in 2018, and 20% in 2019.

LCA 2 was also characterized by three medications: ritonavir (RTV), darunavir (DRV), emtricitabine/tenofovir disoproxil fumarate (FTC/TDF). The drug classes represented are NRTI and boosted PI. This was consistently the smallest class, making up 16%, 11%, and 6% in 2017–2019, respectively.

LCA 3 was the final pattern that was identified each year and was characterized by a single 3-drug medication: dolutegravir/abacavir/lamivudine (DTG/ABC/3TC), which includes drugs that are NRTIs and INSTIs. This pattern made up 37% of the sample in 2017, 15% in 2018, and 30% in 2019.

Table 1 Sample descriptives ($N = 3,552$)

	2017	2018	2019
Viral suppression			
Suppressed	2040 (57.4%)	2075 (58.4%)	1971 (55.5%)
Unsuppressed	1080 (30.4%)	1061 (29.9%)	1044 (29.4%)
Missing	432 (12.2%)	416 (11.7%)	537 (15.1%)
Number of viral load records			
Mean (SD)	3.4 (1.9)	3.2 (1.6)	3.1 (1.5)
No change in suppression	2351 (66.2%)	2422 (68.2%)	2307 (65.0%)
Adherence level			
< 50%	175 (4.9%)	166 (4.7%)	203 (5.7%)
> 50–80%	498 (14.0%)	477 (13.4%)	457 (12.9%)
> 80–90%	412 (11.6%)	452 (12.7%)	401 (11.3%)
> 90–95%	432 (12.2%)	425 (11.7%)	403 (11.3%)
> 95%	1921 (54.1%)	1937 (54.5%)	1963 (55.3%)
Missing	115 (3.2%)	106 (3.0%)	125 (3.5%)
Number of quarters with ART regimen switches			
0 switches	2486 (70.0%)	2195 (61.8%)	2241 (63.1%)
1 switch	611 (17.2%)	685 (19.3%)	704 (19.8%)
2 switches	409 (11.5%)	549 (15.5%)	506 (14.2%)
3 + switches	46 (1.3%)	123 (3.4%)	101 (2.8%)
Mean (SD)	0.441 (0.745)	0.612 (0.891)	0.573 (0.855)
Single-tablet regimen (STR)	1953 (55.5%)	2146 (60.4%)	2498 (70.3%)
Total ART medication fills			
Mean (SD)	19.2 (11.4)	18.2 (10.6)	16.1 (9.4)
Nadir CD4			
>=200	2727 (76.8%)		
< 200	825 (23.2%)		
Number of physical comorbidities			
Mean (SD)	1.55 (1.43)		
Number of mental/behavioral conditions			
Mean (SD)	2.34 (1.98)		
Age categories			
18–29	475 (13.4%)		
30–49	2027 (57.1%)		
50+	1044 (29.4%)		
Missing	6 (0.2%)		
Race/ethnicity			
Non-Hispanic Black	1925 (54.2%)		
Non-Hispanic White	273 (7.7%)		
Hispanic	1258 (35.4%)		
Non-Hispanic Other	80 (2.2%)		
Missing	16 (0.5%)		
Gender identity			
Cis female	1148 (32.3%)		
Cis male	2239 (63.0%)		
Transgender	165 (4.6%)		
Housing status			
Stable housing	3460 (97.4%)		
Unstably housed	92 (2.6%)		

Notes. No change in viral suppression indicates members who were consistently suppressed or consistently unsuppressed based on patient records for the year. Physical comorbidities include endocarditis, asthma, pain, COPD, diabetes, hepatitis C, hypertension, and myocardial infarction. Behavioral health conditions include depression, anxiety, bipolar disorder, schizophrenia, post-traumatic stress disorder, drug use, alcohol use, and opioid use disorder

Table 2 Conditional probabilities of patterns of ART medication by Year

	Name	Drug Class	2017	2018	2019
LCA 1	**DTG + FTC/TAF + DRV/COBI**	INSTI, Combination NRTIs, boosted PI	**26%**	**25%**	**20%**
	DTG	INSTI	*0.56*	*0.61*	*0.68*
	FTC/TAF	Combination NRTIs	*0.45*	*0.57*	*0.55*
	DRV/COBI	Boosted PI	*0.32*	*0.33*	*0.27*
LCA 2	**DRV + RTV + FTC/TDF**	Combination NRTIs & boosted PI	**16%**	**11%**	**6%**
	RTV	Boosted PI	*0.99*	*0.99*	*0.94*
	DRV	Boosted PI	*0.63*	*0.67*	*0.66*
	FTC/TDF	Combination NRTIs	*0.57*	*0.43*	*0.31*
LCA 3	**DTG/ABC/3TC**	Combination NRTIs & INSTI	**37%**	**15%**	**30%**
			0.39	*1.00*	*0.42*
LCA 4	**BIC/FTC/TAF**	Combination NRTIs & INSTI		**26%**	**25%**
				0.31	*1.00*
LCA 5	**EVG/COBI/FTC/TAF**	Combination NRTIs & INSTI		**24%**	**19%**
				1.00	*1.00*
LCA 6	**Miscellaneous**		**21%**		

Notes. LCA 1 & 2 are characterized by three different medications each. LCA 3, 4, and 5 are characterized by single medications. Percentages in bold denote percentage of sample assigned to each latent class. Italics denote item-response probabilities of ART medications that were most divergent among latent classes and used to define each latent class.

Two patterns were identified in years 2018 and 2019, both characterized by single medications. LCA 4 was bictegravir/emtricitabine/tenofovir alafenamide fumarate (BIC/FTC/TAF), constituting a quarter of the sample in 2018 and 2019.

LCA 5 was elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (EVG/COBI/FTC/TAF). This pattern made up 24% of the sample in 2018 and 19% in 2019. Both of these medications are composed of drugs from combination NRTI and INSTI classes.

Finally, LCA 6, identified in 2017 and representing 21% of the sample, was not characterized by any dominant medications.

ART medication patterns and viral suppression

Our preliminary analyses examined each latent class separately using logistic regression to determine whether odds of viral suppression differed by ART adherence level. PWH demonstrating at least 80% adherence (i.e., >80–85% and >85–90%) did not differ significantly from PWH having 90% or higher adherence in odds of maintaining viral, suggesting that adherence levels above 80% may be sufficient to maintain viral suppression [34]. However, these results were not consistent across years for each latent class, nor did we observe notable variations between latent classes. In other words, ART medication patterns did not consistently differ in odds of maintaining viral suppression across adherence levels. We subsequently analyzed the full sample in a single mixed effects logistic regression model to present a more holistic and robust analysis and, importantly, to account for repeated measures over time (Table 3).

Results of the model showed that, using participants with 95% or greater adherence as the reference group, those with at least 90% adherence (i.e., >90–95%) did not significantly differ in odds of maintaining viral suppression (OR=1.20, $p=0.124$). Conversely, participants in all categories with less than 90% adherence demonstrated significantly lower odds of being virally suppressed. These results controlled for ART medication class, as well as health and sociodemographic characteristics. Many of these covariates were also associated with HIV viral suppression. For example, having a nadir CD4 count of less than 200 (OR=0.10, $p<0.001$), regimen switches between quarters (OR=0.72, $p<0.001$), behavioral conditions (OR=0.68, $p<0.001$), and unstable housing (OR=0.46, $p=0.014$) were associated with a significantly lower odds of viral suppression. Further, non-Hispanic Black (OR=0.31, $p<0.001$) and Hispanic (OR=0.52, $p<0.001$) race/ethnicity were also associated with lower odds of viral suppression compared to non-Hispanic White or other racial/ethnic identities.

Discussion

The ART medication patterns that were identified in this real-world sample reflect HIV treatments that are most commonly prescribed, all of which are recent formulations. These patterns comprise drug classes that have been identified as being more "forgiving" of lower adherence (e.g., INSTI, NRTI) than previous generations [9]. Interestingly, the medication patterns did not perfectly align with specific drug classes, but rather were characterized by different combinations of drug classes. It is important to note that these patterns do not necessarily represent regimens; instead, they characterize dominant ART medication combinations that were filled in this sample. We cannot systematically evaluate differences between regimen types given the drug classes

Table 3 Mixed effects logistic regression model estimating odds of HIV viral suppression

	Odds of Viral Suppression		
Predictors	***Odds Ratios***	***CI***	***p***
(Intercept)	58.99	34.90–99.71	< 0.001
Latent classes			
LCA 1: DTG + FTC/TAF + DRV/COBI	0.86	0.62–1.20	0.373
LCA 2: DRV + RTV + FTC/TDF	0.83	0.57–1.20	0.320
LCA 3: DTG/ABC/3TC	0.94	0.68–1.29	0.688
LCA 4: BIC/FTC/TAF	1.07	0.77–1.48	0.684
LCA 5: EVG/COBI/FTC/TAF	0.97	0.72–1.31	0.854
Adherence			
<50%	0.20	0.14–0.29	**< 0.001**
50–80%	0.51	0.41–0.65	**< 0.001**
>80–90%	0.73	0.58–0.92	**0.007**
>90–95%	1.20	0.95–1.52	0.124
Nadir CD4 < 200	0.10	0.08–0.13	**< 0.001**
Physical comorbidities	1.02	0.95–1.10	0.543
Behavioral conditions	0.68	0.65–0.73	**< 0.001**
Quarters regimen switch	0.72	0.66–0.78	**< 0.001**
Age category			
18–29	0.39	0.27–0.55	**< 0.001**
30–49	0.88	0.70–1.11	0.272
Race/ethnicity			
Non-Hispanic Black	0.31	0.21–0.45	**< 0.001**
Hispanic	0.52	0.35–0.76	**0.001**
Gender Identity			
Female/Woman	1.21	0.97–1.52	0.089
Transgender	0.96	0.60–1.52	0.849
Unstably housed	0.46	0.25–0.85	**0.014**
Random Effects			
σ^2	3.29		
$\tau^{00}{}_{\text{Subject}}$	4.34		
ICC	0.57		
N_{Subject}	3296		
Observations	8949		
Marginal R^2 / Conditional R^2	0.236 / 0.671		

Notes. References groups: Latent classes, LCA 6 (miscellaneous); adherence, >95%; age category, >50; race/ethnicity, non-Hispanic White or other race; gender identity, male/man

represented in each of the latent medication classes we identified.

These findings add to a growing body of evidence suggesting that ART adherence levels required for viral suppression in real-world settings corroborate existing clinical benchmarks. Overall, ART medication usage of at least 90% adherence did not differ significantly in odds of maintaining viral suppression from adherence levels of 95% or higher. The observed "forgiveness" of the medications in our sample is likely conservative and may be indicative of different properties, such as resistance patterns and daily pill burden, of modern-day ART formulations [35]. Even lower levels of adherence resulting in viral suppression (e.g., 75%) have been observed in other retrospective observational studies, particularly among those on NNRTI- or INSTI-based regimens [11, 36]. Lower medication adherence thresholds (e.g., 80%) are often applied to other chronic conditions [37].

Importantly, most of the sample was adherent at levels of 90% or greater. Despite the high levels of adherence among this sample, we observed that several health and sociodemographic factors that have been previously identified as risks for low adherence were indeed associated with lower odds of viral suppression. Nadir CD4 count below 200 was consistently associated with reduced odds of viral suppression. Severe damage to the immune system, as evidenced by a past diagnosis of AIDS and/or a nadir CD4 count of less than 200 cells/μL may have lasting effects on PWH health and well-being across the lifespan. Thus, failure to maintain durable viral suppression may be part of a syndrome of poor health among PWH above and beyond ART adherence.

Clinical implications

People are non-adherent due to a variety of interrelated factors. Behavioral health conditions are one of the main contributors to ART nonadherence. One study found that adherence among PWH with depressive symptoms was 42% lower than among those without such symptoms [14]. Substance use disorders are frequently comorbid with depression and other mental health conditions, exacerbating non-adherence and disengagement from care among PWH [38]. Consistent with this literature, in the present study behavioral conditions were associated with lower odds of viral suppression across ART medication patterns.

Unstable housing also increases the likelihood of poor ART adherence [20, 39, 40]. One of the most significant barriers to ART adherence is regimen complexity [41]. Single-tablet regimens (STRs) and other less complex regimens (e.g., long-acting injections) that reduce the likelihood of poor adherence may be particularly effective for populations at risk. Among PWH from a South Carolina Medicaid population, viral suppression was achieved at adherence levels of at least 80% with STRs [42]. Those on multi-tablet regimens required at least 90% adherence to achieve viral suppression, echoing results of this present study. Furthermore, PWH on STRs are more likely to have fewer hospitalizations, and have lower healthcare costs compared with PWH on multi-tablet regimens [43]. Prior research in a population similar to the present study, however, did not find any relationship between polypharmacy (related to HIV and other conditions) and viral suppression [6]. Still, providers might prioritize simpler regimens, such as those with a smaller pill-burden, or focus on minimizing other factors that might lead to poor adherence, such as adverse side effects.

Sociodemographic characteristics are also important factors to consider in the ability to maintain viral suppression. For example, transgender and gender-diverse individuals are more likely to report ART non-adherence due to a high prevalence of experiencing depression, poverty, and discrimination in the healthcare setting [22]. Our sample may not have had enough gender-diverse people to observe these patterns. Still, the present study's findings can be used by clinicians to identify and target at-risk populations to reduce barriers to adherence and engage PWH in continued education about the consequences of low adherence. For example, low adherence is associated with development of drug resistance, which can have long-lasting effects on the efficacy of ART regimens. Patient education and encouragement may also increase PWH's self-esteem and motivation, which have been shown to increase ART adherence [44]. By considering reasons for nonadherence or low adherence (e.g., behavioral health conditions, housing instability), simplifying ART regimens, acknowledging sociodemographic factors (e.g., gender identity), and focusing on patient education and motivation, clinicians can better support patients in achieving and maintaining viral suppression, ultimately improving their health outcomes.

Limitations and future directions

One limitation of this study is its generalizability—although our data did include some individuals in controlled environments (e.g., inpatient hospital settings), as well as a small subsample of unstably housed individuals, it did not include all (e.g., incarcerated individuals) who might have trouble filling prescriptions. These data were obtained from a population in a large city with relatively more resources to address HIV/AIDS than smaller cities or rural areas. Another major limitation is that the latent classes that yielded ART medication patterns do not necessarily represent specific ART regimens. As a result, we were unable to make direct comparisons among medications or regimens. Indeed, although we attempted to address this through our model selection criteria, challenges with interpretation due to model complexity and large numbers of indicator variables are among the disadvantages of LCA.

Likewise, we lacked information about duration of ART treatment, medication dosages, or specific regimen switches, all of which may be associated with viral suppression. For example, the study sample includes newly diagnosed patients who may have experienced only one regimen as well as long-term survivors with a more extensive history of ART. However, we did control for number of regimen switches on a quarterly basis and nadir CD4, which is suggestive of how long PWH have been on ART or have had HIV. Given the complexity of these data, LCA was an innovative method for categorizing the vast array of individual medications used by this real-world, clinical sample into manageable patterns of medication use. Importantly, this novel method highlighted the variety in contemporary ART regimens. Expanding the study period past 2019, though beyond the scope of the present study, would capture newer ART medication and prescription trends. Future work might investigate how switches or transitions in ART medication regimens, particularly those motivated by resistance are associated with viral suppression and other clinical outcomes. Other outcomes, including healthcare utilization (e.g., hospitalizations) and costs, should also be considered in future studies.

Finally, PDC is not a direct measure for medication adherence. Pharmacy refill data, though it may not reflect patients' actual adherence and be an overestimation, is a reliable, widely implemented indirect method of quantifying medication adherence [41, 45]. PDC is also as effective as other adherence measures (e.g., self-report,

electronic monitoring) in predicting HIV viral suppression [24].

Conclusion

Consistent with recent findings on contemporary ART regimens, the ART medication patterns identified among this real-world sample demonstrated viral suppression with at least 90% adherence. These data are more translatable to clinical settings than tightly controlled clinical trials. These findings can inform patient education for PWH, especially those who have difficulty maintaining adherence. Although viral suppression is possible with moderate levels of ART adherence, it is not the only relevant outcome. Increased ART adherence is associated with better patient outcomes, such as reduced likelihood of developing resistance, disease progression, and mortality, as well as lower healthcare costs [46]. Providers should encourage high levels of adherence, but also reassure patients who cannot attain those levels that they can still have good viral load outcomes even if they miss an occasional dose.

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J.K., E.F., A.C., J.E. and M.B.I. contributed to the conceptualization of the study; J.K., J.M and M.B.I contributed to the methodology; J.M and M.B.I. conducted the formal analysis; E.F. and A.C. contributed to data curation; J.M prepared the original draft of the manuscript; J.M., Y.W., J.K., E.F., A.C., J.E., and M.B.I. contributed to editing the manuscript; M.B.I provided supervision of the study; J.E. and M.B.I. acquired funding for this study. All authors have read and approved the final manuscript.

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Data availability
The datasets generated and/or analyzed during the current study are not publicly available due to confidentiality agreement among the collaborators but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Ethical review and approval were waived for this study because this is secondary research for which consent is not required. Patient consent was waived due to this study being secondary research for which consent is not required.

Consent for publication
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Competing interests
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