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Journal AIDS, 36(13) ISSN 0269-9370 Authors Pala, Andrea Norcini Kempf, Mirjam-Colette Konkle-Parker, Deborah et al.

Publication Date 2022-11-01

DOI 10.1097/qad.00000000003342

Peer reviewed



# **HHS Public Access**

Author manuscript *AIDS*. Author manuscript; available in PMC 2023 November 01.

Published in final edited form as:

AIDS. 2022 November 01; 36(13): 1769–1776. doi:10.1097/QAD.00000000003342.

## Intersectional Stigmas are associated with lower Viral Suppression Rates and ART Adherence among Women living with HIV

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### Abstract

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Author roles: ANP, BT, and JT contributed to the study design. ANP and BT conducted the statistical analyses. MCK, DKP, TEW, PCT, GW, TBN, MOJ, SDW, and CHL contributed to data collection. All authors provided critical intellectual content and approved the final version of the manuscript.

**Objectives:** To explore the associations between intersectional poverty, HIV, gender, and racial stigma, adherence to antiretroviral therapy (ART), and viral suppression among women living with HIV (WLHIV).

**Design:** We examined intersectional stigmas, self-report ART adherence, and viral suppression using cross-sectional data.

**Methods:** Participants were WLHIV (N=459) in the Women's Adherence and Visit Engagement, a Women's Interagency HIV Study substudy. We used Multidimensional Latent Class Item Response Theory and Bayesian models to analyze intersectional stigmas and viral load adjusting for sociodemographic and clinical covariates.

**Results:** We identified five intersectional stigma-based latent classes. The likelihood of viral suppression was approximately 90% lower among WLHIV who experienced higher levels of poverty, gender, and racial stigma or higher levels of all intersectional stigmas compared with WLHIV who reported lower experiences of intersectional stigmas. ART adherence accounted for but did not fully mediate some of the associations between latent intersectional stigma classes and viral load.

**Conclusion:** The negative impact of intersectional stigmas on viral suppression is likely mediated, but not fully explained, by reduced ART adherence. We discuss the research and clinical implications of our findings.

### Introduction

Women living with HIV (WLHIV) account for nearly one-fourth of persons living with HIV (PLWH) in the US.[1] WLHIV have lower rates of viral suppression, particularly Black and Latina living in disadvantaged socioeconomic conditions.[2–5] HIV stigma significantly contributes to these disparities and its effect is likely exacerbated by co-occurring forms of stigma.[6] For example, stigmas based on race, gender, and poverty have been associated with lower viral suppression rates and antiretroviral therapy (ART) levels [7–10], although they have been examined individually. To date, few studies have investigated the combined effect of intersectional stigmas on ART adherence and viral suppression remains poorly understood.[11]

The intersectionality framework suggests that stigmas based on multiple stigmatized identities operate synergistically to affect wellbeing and health outcomes.[11, 12] Stigmatized identities are characteristics deemed undesirable by society that leads to loss of social status and multiple forms of oppression.[6] The intersection of multiple stigmatized identities uniquely shapes WLHIV's lived experiences and the effect on ART adherence and HIV treatment outcomes.[13, 14] Genderism, for example, adds to the burden of HIV stigma faced by WLHIV. Racism selectively affects Black and Latina WLHIV. The effect of these experiences goes beyond the sum of their individual effects, as they operate in a complex, multiplicative fashion.[11, 13] As the experiences of intersectional stigmas accumulate, they may adversely affect multiple life domains, health-related behaviors, and ultimately health outcomes.

This study explored differences in viral suppression rates and ART adherence among WLHIV with different combinations and levels of experienced intersectional stigmas. We also explored the role of ART adherence in accounting for the association between intersectional stigmas and viral suppression.

### Methods

### Recruitment

Participants were WLHIV in the Women's Adherence and Visit Engagement (WAVE) sub-study of the Women's Interagency HIV Study (WIHS).[15] Women were enrolled in the WAVE sub-study at four WIHS sites to represent different parts of the country: Birmingham, AL and Jackson, MS to represent the Deep South; Atlanta, GA to represent the Southeast; and San Francisco, CA to represent California. Participants provided written informed consent, and study procedures were approved by the WIHS Executive Committee and the Institutional Review Boards at each participating WIHS site. Participants completed interviewer-administered quantitative assessments. Blood samples were collected to assess viral load. The collection of the data used in this study took place between April 2016 and April 2017.

### Measures

Experienced intersectional stigmas consisted of questionnaires assessing discrimination, unfair treatment, exclusion, and devaluation from others in diverse social contexts in the past 12 months.

*Experienced poverty stigma* was assessed using the 4-item subscale of the perceived poverty stigma[16] including *I have found that people say negative or unkind things about me behind my back because of my financial situation.* and *I have been excluded from work, school, and/or family functions because of my financial situation.* Items were rated on a 5-point scale (from *Definitely Disagree* to *Definitely Agree*). In this sample, the subscale internal reliability was good ( $\alpha = 0.87$ ). Higher scores corresponded to a greater level of experienced poverty stigma.

<u>Experienced HIV stigma</u> was assessed with the 12-item subscale of the HIV Stigma Scale. [17] Items included, for example, *I have been hurt by how people reacted to learning I have HIV*, and *People have physically backed away from me when they learn I have HIV*. Items were rated on a 4-point scale (from *Strongly Disagree* to *Strongly Agree*). The subscale internal reliability in this study was excellent ( $\alpha = 0.94$ ). Higher scores corresponded to a greater level of experienced HIV stigma.

*Experienced racial stigma* was assessed using the experiences of discrimination scale.[18] Two of the 10 items of the scale were highly correlated (polychoric correlation = 0.98), specifically the items assessing the experience of racial stigma in medical settings and experience of racial stigma in a store or restaurant. The endorsement of the item on the experience of racial stigma in a store or restaurant was low (n=11, 2.4%). Because of the high correlation between two items and low endorsement of one of the items, the model did not converge. Thus, we removed the item on the experience of racial stigma in a store or

restaurant to improve model convergence. In total, we used nine of the original 10 items, eight items assessed lifetime experiences of racial discrimination on a 4-point scale (*Never*, *Once, Two or three times*, and *Four or more times*); one item assessed global experience of racism (i.e., *How often do you feel that you, personally, have been discriminated against because of your race, ethnicity, or color?*) on a 4-point scale (from *Never* to *Often*). In this study, the internal reliability of the 9-item scale was acceptable ( $\alpha = 0.76$ ). Higher scores corresponded to elevated racial stigma experiences.

*Experienced gender stigma* assessment comprised the 13-item scale Schedule of Sexist Events.[19] Participants were asked how often, as a woman, for example, *Have been denied a raise, promotion, a job or something at work you deserved?, Have been called a sexist name like bitch, cunt, chick, or other names?* Each item was rated on a 4-point scale from Never to Often. In this study, the internal reliability was good ( $\alpha = 0.86$ ). Higher scores corresponded to greater experienced gender stigma levels.

*Viral suppression* was assessed using viral load tests run as part of the WIHS study. Viral load <20 copies/mL was coded 1 (i.e., viral suppression), whereas viral load >20 copies/mL was coded as 0 (i.e., detectable viral load).

*ART adherence* was evaluated using a self-report 1-item measure. Participants were asked how often they took ART as prescribed over the past 6 months. Response options included, "100% of the time", "95–99% of the time", "75–94% of the time", "<75% of the time", and "I haven't taken any of my prescribed medications." Previous studies support the validity of this 1-item assessment.[20–22] We dichotomized the variable to create two categories, 0 - 95% or higher vs. 1 - lower than 95%.[20, 21] We chose a 95% cut-off based on studies showing that more "forgiving" adherence levels ( 80%) leading to viral suppression are associated with higher residual viral load, inflammation, immune activation, risk of coagulopathy, and mortality.[23–25]

*Sociodemographic characteristics* included age at visit, race (Latina vs. Non-Latina), ethnicity (white, African American/black, other), income (\$12,000 or less, \$12,001–24,000, \$24,001–36,000, \$36,001 or more), education (<High school/GED, High school/GED, Some college/Associate, College and above).

### Data analysis plan

We used R Studio (Version 1.4.1717)[26] to perform statistical analyses. Associations between groups based on intersectional stigmas (i.e., latent classes) and categorical variables were tested using chi-square tests (e.g., viral suppression). Associations with ordinal variables were examined with the Kruskal-Wallis test (e.g., income). ANOVA was used to test differences across intersectional stigmas groups. We used *psych* package[27] to calculate Cronbach's a to estimate the internal reliability of stigma measures.

We used Multidimensional Latent Class Item Response Theory (MLCIRT) to identify groups of participants with different combinations of four intersectional stigmas, which were modeled as distinct latent traits. Latent traits are modeled as standardized continuous variables – mean=0 and SD=1. The latent trait-item relationship was assessed using

two parameters: discrimination and location. The discrimination parameter estimates the precision with which a given item correctly discriminates between individuals with higher or lower latent trait scores (i.e., levels of experienced stigma). Commonly, the discrimination parameters range between |1| and |4|, with values closer to 4 indicating a greater precision in identifying individuals with high/low levels of experienced stigma. Location parameters identify the latent trait score (i.e., level of experienced stigma) above which the probability of endorsing a given item is >50%. Location parameters commonly range from -3 to +3.

Compared to latent profiles/class analysis (i.e., based on continuous or dichotomized raw stigma scores), MLCIRT offers several advantages, it accounts for the multidimensionality of class indicators (i.e., experienced stigma items), the unique contribution of each item in measuring the underlying latent trait (experienced stigma), and measurement error ( i.e., items' variance unrelated to latent traits). We used *MLCIRTwithin*[28] package to perform MLCIRT. Fit indices used to select the optimal class number included Bayesian Information Criterion (BIC), sample adjusted BIC (aBIC), Akaike Information Criterion (AIC), and Vuong-Lo-Mendell-Rubin likelihood ratio test (LRT).[29, 30] Lower BIC, aBIC, and AIC values indicate a good model fit. The LRT compares nested models N-class vs N-1-class, where a significant LRT indicates a better fit of the N-class model. Finally, the selection of the model to select was also determined by the sizes and interpretability of the classes.[29]

We explored the association between intersectional stigmas (i.e., latent classes), ART adherence, and HIV treatment outcomes using Bayesian Structural Equation Model (BSEM), *brms* package.[31] BSEM allowed us also to estimate indirect associations between the groups and viral suppression with appropriately asymmetric credible intervals. We used logistic regression models based on the Bernoulli distribution and uninformative diffuse priors.[31] We estimated cross-sectional indirect associations to explore the role of ART adherence in explaining the differences in viral suppression across the groups based on intersectional stigmas. We reported 95% Bayesian confidence intervals for all odds-ratio estimates, adjusted for covariates including age, race, ethnicity, education, income, and months since ART initiation.

**Mediation analysis:** We calculated the direct, indirect, and total odds-ratio estimates using the package bayestestR,[32] which implements an algorithm providing a robust estimation of indirect associations compared to the product-of-pathways method. We used the Equal-Tailed Interval (ETI) method to calculate indirect associations and confidence intervals.[32]

We used posterior membership probability to test the association between latent classes based on experienced intersectional stigmas, ART adherence, and viral suppression. MLCIRT estimates participants' membership probability for each latent class. For example, a participant may have a 0.5 probability of being in a hypothetical Class 1, 0.3 probability of being in Class 2, and 0.2 probability of being in Class 3. Another person may have 1.00 probability of being in Class 1 and 0 probability of being in any of the other classes. The use of posterior membership probability in regression analysis allows accounting for membership uncertainty. The class with the lowest levels of experienced stigma was used as the reference group.

Missing data were accounted for at each stage of the analysis. MLCIRT is based on maximum likelihood estimation, which uses the full information (FIML) approach to handle missing data. BSEM was performed on 100 multiple imputations, as brms package requires complete case data as input. We imputed missing data using Multivariate Imputation by Chained Equations with mice[33] package in R.

### Results

### Sample characteristics

Sociodemographic and clinical characteristics of study participants (N=459) are shown in Table 1. Participants were on average 49.06 years old, approximately 15% were White, and more than 90% were non-Latina. More than half of the participants reported an income of \$12,000 or less, and the highest level of education was High school/GED or lower. On average, participants were on ART for 103.74 months (8 years, approximately), more than two-thirds of them were virally suppressed, and more than 80% reported optimal ART adherence. For descriptive purposes, we report summary statistics of the experienced intersectional stigmas measures' raw score although multidimensional latent class models will be based on latent traits. Because of the stigma measures' differences in the number of items and response options, the mean of the raw scores cannot be compared (Table 1).

#### Intersectional stigmas - Multidimensional latent class models

The IRT component of MLCIRT was confirmatory, whereas the latent class component was exploratory because we did not have a-priori hypotheses about the number of classes. We estimated and compared fit indices of 2- to 6-class nested models (Table S1; the 7-class model did not converge). Although the 6-class model was the best fitting model (i.e., lower BIC, aBIC, and AIC and statistically significant LRT), we chose the 5-class model because the extra class in the 6-class model did not add significant information compared with the 5-class model. The two models (5- vs. 6-class) showed nearly identical patterns of experienced stigmas and one of the six classes was relatively small (n=28, 6%).

In Figure 1 we reported the standardized levels of experienced stigma by class. We labeled the five classes according to the unique combinations of experienced stigma types and levels: Class 1) Low poverty, HIV, gender, and racial stigma; Class 2) Moderate HIV and poverty stigma; Class 3) Higher poverty, gender, and racial stigma; Class 4) Higher HIV and poverty stigma; Class 5) High poverty, HIV, gender, and racial-stigma. We used the sample mean (i.e., 0) as a reference to determine Low, Moderate, and High levels of experienced stigmas for each class.

Nearly all items assessing experienced intersectional stigmas showed discrimination parameters above one, suggesting that each item accurately identified participants with different levels of a given stigma. Location parameters of questionnaires measuring poverty, HIV, and gender stigma indicated that each item captured a wide range of experienced stigma. For example, the location parameters of the item *I have been hurt by how people reacted to learning I have HIV* were –2.225 (Strongly Disagree vs. Disagree), –0.310 (Disagree vs. Agree), and 1.746 (Agree vs. Strongly Agree). Because the underlying trait

is standardized (mean=0, and SD=1), individuals who endorsed Strongly Disagree may be placed -2.225 standard deviations below the latent trait mean (low level of experienced HIV stigma). Endorsement of the option Disagree would place participants between -2.225 standard deviations and -0.310 standard deviations from the mean, namely closer to the sample mean levels of experienced HIV stigma but still on the lower side. Experienced racial stigma items were associated with location parameters greater than 0, indicating that they are more sensitive to higher levels of experienced racism. Only the item *How often do you feel that you, personally, have been discriminated against because of your race, ethnicity, or color?* was associated with a location parameter lower than 0. When most items of a questionnaire assess events with low probabilities (e.g., rare events), their location parameters tend to be above 0. Indeed, 32.0% of the participants did not report any racial stigma experience, whereas a smaller proportion did not experience poverty (15.9%), gender (9.4%), or HIVstigma (4.4%).

# Sociodemographic and HIV clinical and behavioral variables by intersectional stigmas latent classes – Bivariate analysis

The groups' size was, Class 1 n=90; Class 2 n=102; Class 3, n=123; Class 4, n=80; Class 5, n=64. We found statistically significant differences in months since ART initiation, ART adherence, and viral load suppression across the five groups, but not on race, ethnicity, age, education, and average yearly household income (Table S2).

### Intersectional stigma, ART adherence, and viral suppression

We tested the theoretical model in Figure S1 using BSEM. Analysis was adjusted for: age, race/ethnicity, education, income, and months since ART initiation (Figure S2). The low poverty, HIV, gender, and racial stigma class was used as a reference group as it showed better ART adherence and viral load compared with other classes (Table S2).

**Intersectional stigmas and ART adherence.**—Compared with the reference group, the odds of ART adherence 95% were significantly lower for WLHIV in the higher poverty, gender, and racial stigma (Class 3) or high poverty, HIV, gender, and racial stigma (Class 5). The odds of ART adherence 95% were 66.5% (p<0.01) and 75.2% (p<0.01) lower, respectively.

**Intersectional stigmas and viral suppression.**—Compared with the reference group, WLHIV who endorsed higher poverty, gender, and racial stigma (Class 3) or higher poverty and HIVstigma (Class 4) had 53.5% and 57.2% lower (p<0.05; Table 2) odds of viral suppression, respectively. ART adherence was associated with 4.490-fold higher odds of viral suppression (p<0.001). Because ART adherence was included in the model, the lower odds of viral suppression among WLHIV in Class 3 and Class 4 are not fully explained by ART adherence.

Indirect association between intersectional stigmas and viral suppression through ART adherence.—The lower odds of ART adherence among WLHIV who endorsed higher poverty, gender, and racial stigma (Class 3) or high poverty, HIV, gender,

and racial stigma (Class 5) resulted in 79.3% (p<0.05) and 86.8% (p<0.01) lower odds of being virally suppressed, respectively (Table 3).

Table 3 shows the total effects, which combine the direct and indirect associations (through ART adherence) that quantify the odds of viral suppression of the five classes. Because of low ART adherence, WLHIV who experienced higher poverty, gender, and racial stigma (Class 3) or experienced elevated levels of all intersectional stigmas (Class 5) were less likely to be virally suppressed (90.5% and 90.4%, respectively) compared with participants in the reference group. Finally, ART adherence did not account for the lower odds of viral suppression among women with higher poverty and HIV stigma (Class 4).

### Discussion

In this study, we identified five groups of WLHIV based on unique combinations of stigmas (i.e., based on HIV, poverty, gender, and race), which have been individually associated with non-adherence to ART and detectable viral load in previous studies. [9, 34] The five groups we have identified were differently associated with ART adherence and detectable viral load, whereas they did not differ in sociodemographic characteristics, likely due to the relatively homogenous sample. For example, more than 85% of the participants were non-Latina and Black and nearly 80% of them reported low income (<24k).

Our findings may support the hypothesis that the adverse effect of HIV stigma on HIV treatment outcomes may be exacerbated by concurrent experiences of other forms of stigma. [6] We found that WLHIV who experienced higher stigma based on poverty, gender, and race or stigma based on poverty and HIV have a higher likelihood of detectable viral load regardless of ART adherence.[35] Because we accounted for ART adherence, these associations might be mediated by additional mechanisms (e.g., chronic inflammation, substance use, chronic stress).[7, 36, 37]

WLHIV who experienced severe levels of three or more forms of stigma have more than 66% probability of being non-adherent to ART compared with the reference group. These findings might suggest that the intensity of experiences of intersectional stigmas significantly impacts ART adherence. Additional studies are needed to explore potential mediators such as social support (or lack thereof), coping strategies, mental health, and substance use. In our study, WLHIV who experienced HIV and poverty stigma were not less likely to be adherent to ART, but they might be at risk of depressive symptoms, which would ultimately interfere with ART adherence.[8, 38]

The mediation analysis further confirmed that ART adherence contributes but does not fully explain the effect of intersectional stigmas on viral suppression. Due to low ART adherence, WLHIV who reported higher experiences of all intersectional stigmas were 86.8% more likely than women who experienced low intersectional stigma to have a detectable viral load. Likewise, the combination of gender, racial, and poverty stigma might reduce the likelihood of viral suppression by 79.3% through non-adherence to ART.

Our study is one of the first to evaluate intersectional stigmas through MLCIRT and explore its association with ART adherence and HIV treatment outcomes. MLCIRT is an innovative

analytical approach that integrates variable- and person-centered methods.[28] MLCIRT hypothesizes a non-linear relationship between the traits assessed,[28] which is a key intersectionality concept.[7, 11, 28, 39, 40] Our study contributes significantly to knowledge of methodological approaches to address non-additive/linear effects[11] to examine the complexity of intersectional stigmas.[35] We have examined the relationship between ART adherence and viral load with different combinations of stigmas that have been previously linked (individually) to detectable viral load.[7–10]

Our study has some limitations. The sample is a non-probability sample, so inferences may not generalize fully to WLHIV in other settings and contexts. The findings of cross-sectional data cannot be used to infer the causality or directionality of the associations examined, especially for mediation effects. Self-reported ART adherence is subject to social desirability and recall biases, which may be reduced using objective, innovative measures of adherence including ART hair levels. In our study, participants may have underreported racial stigma experiences or may have experienced other types of racial stigmatization (microaggression), which our questionnaire did not capture.[41] Despite these limitations, our study features an objective outcome measure and provides important, innovative findings contributing to understanding the ways that intersectional stigmas operate on HIV treatment outcomes.

In conclusion, our findings suggest that different combinations of experienced intersectional stigmas might adversely affect HIV treatment outcomes. The experience of moderately high levels of some of the intersectional stigmas might be as harmful as experiencing elevated levels of all intersectional stigmas. This finding reflects the focus of intersectionality frameworks on assessing the synergistic experiences of stigma.[11] ART adherence plays a key role in explaining the link between experienced intersectional stigmas and HIV treatment outcomes but does not fully explain it. Other potential mechanisms may explain the effect of intersectional stigmas on viral load including chronic stress, mental health, and substance use. Our study findings have important implications for future research and potentially clinical practice. We used an innovative method that accounts for unobserved inter-individual differences in the levels of experienced intersectional stigmas. Our results suggest that health providers may identify WLHIV at high risk for non-adherence and detectable viral load using self-report measures of experienced intersectional stigmas. IRT findings support the use of the scales to assess poverty, HIV, and gender stigma, whereas the racial stigma scale may produce a limited estimation of experienced racism.

### **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

### Acknowledgements:

The authors gratefully acknowledge the contributions of the study participants and the dedication of the staff at the MWCCS sites.

#### Sources of support:

The contents of this publication are solely the responsibility of the authors and do not represent the official views of the National Institutes of Health (NIH). MWCCS (Principal Investigators): Atlanta CRS (Ighovwerha Ofotokun, Anandi Sheth, and Gina Wingood), U01-HL146241; Data Analysis and Coordination Center (Gypsyamber

D'Souza, Stephen Gange and Elizabeth Golub), U01-HL146193; Northern California CRS (Bradley Aouizerat, Jennifer Price, and Phyllis Tien), U01-HL146242; UAB-MS CRS (Mirjam-Colette Kempf, Jodie Dionne-Odom, and Deborah Konkle-Parker), U01-HL146192. The MWCCS is funded primarily by the National Heart, Lung, and Blood Institute (NHLBI), with additional co-funding from the Eunice Kennedy Shriver National Institute Of Child Health & Human Development (NICHD), National Institute On Aging (NIA), National Institute Of Dental & Craniofacial Research (NIDCR), National Institute Of Allergy And Infectious Diseases (NIAID), National Institute Of Neurological Disorders And Stroke (NINDS), National Institute Of Mental Health (NIMH), National Institute On Drug Abuse (NIDA), National Institute Of Nursing Research (NINR), National Concer Institute (NCI), National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institute on Deafness and Other Communication Disorders (NIDCD), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute on Minority Health and Health Disparities (NIMHD), and in coordination and alignment with the research priorities of the National Institutes of Health, Office of AIDS Research (OAR). MWCCS data collection is also supported by UL1-TR000004 (UCSF CTSA), P30-AI-050409 (Atlanta CFAR), and P30-AI-027767 (UAB CFAR). The work of Dr. Norcini Pala is supported by K01-MH125724 (NIMH).

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### Figure 1:

Experienced Poverty-, HIV-, Gender-, and Racial-Stigma by Class.

### Table 1.

### Participants' Sociodemographic and HIV Clinical Biomarkers

	Overall
	N=459
Age (mean (SD))	49.06 (9.45)
White, n (%)	68 (14.8)
Non-Latina, n (%)	426 (92.8)
Highest level of education, n (%)	
1. <high ged<="" school="" td=""><td>129 (28.6)</td></high>	129 (28.6)
2. High school/GED	141 (31.3)
3. Some college/Associate	142 (31.5)
4. College and above	39 (8.6)
Highest level of education, median (IQ)	2 [1, 3]
Average yearly household income, n (%)	
1. \$12,000 or less	250 (57.1)
2. \$12,001–24,000	99 (22.6)
3. \$24,001–36,000	42 (9.6)
4. \$36,001 or more	47 (10.7)
Average yearly household income, median [IQ]	1 [1, 2]
Viral load suppression (<20 copies/ml), n (%)	305 (67.6)
95% ART adherence over past 6 months, n (%)	350 (82.2)
Time since ART initiation, months (mean (SD))	103.74 (71.58)
Experienced intersectional stigmas raw scores (mean (SD))	
Poverty	6.05 (4.24)
HIV	16.44 (8.75)
Gender	9.07 (7.15)
Racial	2.21 (2.99)

IQ = interquartile range

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# Table 2.

Direct Association Between Intersectional Stigmas, Viral Suppression, and ART Adherence - Bayesian Structural Equation Model (N=459; Supplementary Figure S2)

	ART adherence 95%	Viral suppression (<20 copies/ml)
	aOR (95% CI)	aOR (95% CI)
ART adherence 95%		4.490(2.580 –7.940) ***
Lower poverty, HIV, gender, racial stigma (re	f. group)	
Moderate poverty and HIV stigma	0.583(0.210 - 1.525)	0.761(0.357 - 1.594)
Higher poverty, gender, and racial stigma	$0.335(0.127-0.801)^{**}$	$0.465 (0.229 - 0.910)^{*}$
Higher poverty and HIV stigma	0.693(0.232–2.024)	$0.428(0.199-0.892)^{*}$
High poverty, HIV, gender, racial stigma	$0.248(0.089-0.650)^{**}$	0.742(0.324–1.707)
* p 0.05		
** p 0.01		
*** p 0.001		

Covariates were included as predictors of viral suppression and ART adherence 95%; aOR = adjusted odds-ratio.

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# Table 3.

Indirect Association Between Intersectional Stigmas and Viral Suppression through ART Adherence - Bayesian Structural Equation Model (N=459; Supplementary Figure S2)

	Viral suppression (<20 copie	es/ml)
	Indirect association via ART adherence 95%	Total association
	aOR (95% CI)	aOR (95% CI)
Lower poverty, HIV, gender, racial stigma (ref. group)		
Moderate poverty and HIV stigma	0.465(0.076–1.752)	0.35(0.053-1.630)
Higher poverty, gender, and racial stigma	0.207(0.029–0.659) *	$0.095(0.015-0.401)^{***}$
Higher poverty and HIV stigma	0.591(0.094–2.769)	0.251(0.036 - 1.370)
High poverty, HIV, Gender, racial stigma	$0.132(0.016{-}0.493)^{**}$	$0.096(0.013-0.493)^{**}$

\*\* p 0.01

AIDS. Author manuscript; available in PMC 2023 November 01.

Covariates were included as predictors of viral suppression and ART adherence 95%; aOR = adjusted odds-ratio; Total association combines direct and indirect associations.