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High Levels of Syndemics and Their Association with Adherence, Viral Non-suppression, and Biobehavioral Transmission Risk in Miami, a U.S. City with an HIV/AIDS Epidemic

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Abstract

Miami is a Southeastern United States (U.S.) city with high health, mental health, and economic disparities, high ethnic/racial diversity, low resources, and the highest HIV incidence and prevalence in the country. Syndemic theory proposes that multiple, psychosocial comorbidities synergistically fuel the HIV/AIDS epidemic. People living with HIV/AIDS in Miami may be particularly affected by this due to the unique socioeconomic context. From April 2017 to October 2018, 800 persons living with HIV/AIDS in a public HIV clinic in Miami completed an interviewer-administered behavioral and chart-review cross-sectional assessment to examine the prevalence and association of number of syndemics (unstable housing, low education, depression, anxiety, binge drinking, drug use, violence, HIV-related stigma) with poor ART adherence, unsuppressed HIV viral load (≥ 200 copies/mL), and biobehavioral transmission risk (condomless sex in the context of unsuppressed viral load). Overall, the sample had high prevalence of syndemics ($M = 3.8$), with almost everyone (99%) endorsing at least one. Each syndemic endorsed was associated with greater odds of: less than 80% ART adherence (aOR 1.64, 95% CI 1.38, 1.98); having unsuppressed viral load (aOR 1.16, 95% CI 1.01, 1.33); and engaging in condomless sex in the context of unsuppressed viral load (1.78, 95% CI 1.30, 2.46). The complex syndemic of HIV threatens to undermine the benefits of HIV care and are important to consider in comprehensive efforts to address the disproportionate burden of HIV/AIDS in the Southern U.S. Achieving the 90-90-90 UNAIDS and the recent U.S. "ending the epidemic" targets will require efforts addressing the structural, social, and other syndemic determinants of HIV treatment and prevention.

Keywords HIV/AIDS · Syndemics · Adherence · Unsuppressed virus · Biobehavioral transmission risk

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Introduction

Human immunodeficiency virus (HIV) infections have shown overall declining rates in the United States (U.S.) [1] and advances in antiretroviral treatment (ART) have made it possible for adherent persons living with HIV/AIDS to maintain HIV viral suppression. Virally suppressed individuals are not able to transmit the virus and have markedly improved life expectancies [2–7]. In addition to ART treatment as prevention (TasP), the advent of pre-exposure prophylaxis (PrEP) has made a significant contribution to primary prevention of HIV [8]. Despite the overall decreasing rates and unprecedented developments in care and prevention, select geographic regions continue to struggle with continued high rates of HIV and poor HIV/AIDS treatment outcomes.

In particular, the Southern region of the U.S. makes up the majority of new HIV diagnoses (52%) with incidence remaining stable from 2012 to 2016 [9]. The South also has significant prevalence and HIV mortality; in 2015, the South contained 46% of individuals living with HIV in the U.S. and about half of the deaths among people living with HIV (47%). Examining differences within this high-risk geographic area, people of color are disproportionately burdened by HIV making up 77% of new diagnoses in 2017. Specifically, Black, non-Hispanic/Latinx individuals had the highest burden followed by Hispanic/Latinx individuals. Additionally, the Southeastern states of Florida, Georgia, and Louisiana have even higher rates of HIV diagnoses compared to their Southern state counterparts with the state of Florida containing the majority of the HIV "hot spots" (i.e., ranked within the top 10 for incidence and prevalence) including Miami, Orlando, and Jacksonville [9, 10]. Notably, Miami has the highest HIV incidence, the highest HIV prevalence, and is among the top three U.S. cities with the highest AIDS prevalence [9]. In addition, Miami is a city with high health and economic disparities, high ethnic/racial diversity, and relatively low resources compared to other areas of the U.S. making the HIV/AIDS epidemic similar to many developing regions with uncontrolled HIV across the globe [11, 12]. Given this increasing epidemic, understanding factors driving HIV/AIDS within Miami's unique context is urgent to begin to intervene and mitigate the current public health crisis.

Syndemic theory proposes that multiple, co-occurring psychosocial comorbidities act synergistically to fuel the HIV/AIDS epidemic [13]. In other words, HIV is not a siloed issue, but rather driven by the interrelatedness of disease, mental health, behavior, and social and structural conditions. The complexity of syndemic factors results from the fact that syndemic conditions operate on multiple levels including intrapersonal, interpersonal, community, societal, and structural levels. Examples of syndemic conditions that have been explored as reinforcing HIV risk include depression, substance use, violence (abuse/trauma), stigma, unstable housing, food insecurity, and poverty [14–16]. To date, syndemic theory has primarily been used to contextualize HIV acquisition risk among high-risk groups, especially among men who have sex with men [17, 18]. Such research has established a well-supported link between syndemic conditions and HIV risk, including a positive dose–response relationship between number of syndemic conditions and seroconversion [16, 19, 20].

The syndemic conditions of depression, substance use, stigma, trauma, violence, and socioeconomic marginalization have been established as independent risk factors for poor HIV outcomes [21–26]. For example, in a prospective study, depression was a significant predictor of a greater rate of CD4+ T cell count decline and increase in HIV viral load [27]. Compared to non-users, all individuals who were using drugs, regardless of pattern of use (e.g., intermittent use, persistent use), had greater odds of having unsuppressed viral load [28] and increases in alcohol drinking significantly predicted lower odds of improving ART adherence and being virally suppressed [29]. Further, stigma, experiencing intimate partner violence, and trauma exposure have also been associated with poor ART adherence and lower odds of viral suppression [21, 30, 31]. Low education and housing instability, indicators of low socioeconomic status, have been associated with faster disease progression, difficulty sustaining viral suppression, poor ART adherence, and overall greater risk of forward transmission [32, 33]. Although these factors have been associated with poor HIV outcomes and subsequent consequences for secondary prevention, research examining the prevalence and correlates of syndemics in people living with HIV/AIDS is relatively understudied. Among persons living with HIV/AIDS, the number of experienced syndemic conditions is associated with lower rates of viral suppression, detectable viral load, decreased medication adherence, and increased healthcare utilization [34–43]. It is especially noteworthy that only one of these studies [43] has been conducted in the Southeastern U.S., and, as discussed above, the Southeastern region of the U.S. is an area in which psychosocial syndemics are high, resources are low, and there is a disproportionate burden of HIV compared to other regions of the country [10].

The present study sought to address this gap by examining the prevalence and correlates of syndemics among persons living with HIV/AIDS who may be at risk for falling off different components of the HIV care continuum: patients receiving care at a public HIV care clinic in Miami. Specifically, we examined the association between the number of syndemics experienced and ART adherence, viral nonsuppression, and, given the importance of treatment as prevention, HIV transmission risk behavior in the context of unsuppressed viral load (i.e., biobehavioral transmission risk).

Methods

Participants and Procedures

From April 2017 through October 2018, 800 persons living with HIV/AIDS in a public, non-profit tertiary care hospital in downtown Miami completed a one-time interviewer-administered psychosocial assessment in either English or Spanish. Inclusion criteria included: (a) clinic patient receiving HIV care, (b) able to give consent, (c) 18 years of age or older, and (d) able to speak and understand either English or Spanish. Viral load data was extracted from medical charts per consent from patients. All study procedures received approval from the University of Miami Institutional Review

Board prior to study onset. Informed consent was obtained from all individual participants included in the study.

Measures

Demographics

Age, race/ethnicity, gender, sexual orientation, and relationship status were collected.

HIV Biomarkers

Viral load was extracted from electronic medical records and unsuppressed virus was defined as ≥ 200 copies/mL, the clinical point at which transmission may potentially occur (i.e., individuals with < 200 copies/mL cannot transmit the virus) per the Prevention Access Campaign's Undetectable = Untransmittable consensus statement [44].

Syndemic Conditions

Conditions chosen reflect the syndemic framework which posits that factors at multiple levels, such as intrapersonal (i.e., depression, anxiety, alcohol use, drug use), interpersonal (violence, abuse, trauma), societal (stigma), and structural (low education, unstable housing), drive disease outcomes. Further, conditions were chosen because they have shown independent associations with HIV disease outcomes including poor ART adherence, greater HIV symptoms, decreased CD4 + T-cell count, and increased viral load [21, 27–33, 45].

1. *Depression* The 9-item Patient Health Questionnaire [46] was used to assess depressive symptoms reflecting major depression diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders V [47]. Participants endorsed how often a symptom bothered them on a scale from 0 (*not at all*) to 3 (*nearly every day*). Items are summed with greater scores indicating greater depressive symptoms. A dichotomous depression syndemic condition variable was created by scoring an individual positive if they indicated clinically relevant depression (score of 5 or greater).

2. *Anxiety* The anxiety thermometer was adapted from the National Comprehensive Cancer Network Distress Thermometer [48], a single item self-report measure assessing distress using a visual analog scale from 0 (*no distress*) to 10 (*extreme distress*). For the current study, the word distress was replaced with "anxiety" so as not to overlap with the questions on the Patient Health Questionnaire. A dichotomous anxiety syndemic condition variable was created by scoring an individual positive

if they indicated clinically relevant anxiety (a score of 4 or greater) [49, 50].

3. *Alcohol use* Substance use was assessed using a measure adapted from the Addiction Severity Index—Lite [51]. Frequency of use in the past 30 days was assessed for alcohol, marijuana, crack, cocaine, heroin, other opioids, amphetamines, hallucinogens, ecstasy/MDMA, sedatives/tranquilizers, and other drugs (0 = no use, 1 = 1 to 2 times, 2 = about once a week, 3 = several times a week, 4 = about every day). Additionally, for those reporting drinking, average number of daily drinks was assessed. An alcohol use syndemic condition variable was created by scoring an individual positive if they reported any binge drinking (4 or more daily drinks) in the past 30 days.

4. *Drug use* A drug use syndemic condition variable was created by scoring an individual positive if they reported any drug use in the past 30 days.

5. *Violence* A 9-item adaptation of the Intimate Partner Violence Screening Tool [52] was used to assess lifetime childhood abuse, abuse experienced as an adult, and abuse in the context of a romantic relationship. An adaptation of the Brief Trauma Questionnaire [53] assessed lifetime trauma exposure. A violence syndemic condition variable was created by scoring an individual positive if they reported any abuse or trauma.

6. *HIV-related stigma* The 6-item Internalized AIDS-Related Stigma Scale [54] was used to assess participant's perceived stigma associated with their own HIV status. Participants endorsed whether they agreed or not with statements regarding how they feel about their HIV status (e.g., *Being HIV positive makes me feel dirty, I am ashamed that I am HIV positive*). Patients endorsing at least one stigma item scored positive for the stigma syndemic condition variable.

7. *Unstable housing* Patients were identified as positive for unstable housing if they reported homelessness or temporary/transitional housing in the past 12 months.

8. *Low education* Patients were identified positive for low education if they reported less than a high school education.

Number of syndemic conditions All dichotomous syndemic condition variables were summed (range 0 to 8) with greater scores indicating greater conditions experienced.

ART Adherence

A single item from Wilson et al.'s [18] 3-item adherence measure (*In the last 30 days, on how many days did you miss at least one dose of any of your HIV medicines?*) was used to calculate percentage of ART adherence for the past

month. Patient's past month adherence was rated on a scale from 0% (missed all doses) to 100% (perfect adherence). A dichotomous variable representing nonadherence (< 80%) was created.

Biobehavioral Transmission Risk Behavior

A sexual behavior questionnaire assessed types of sexual partners (partner's gender identity and anatomy), type of sex (anal insertive, anal receptive, or vaginal), condom use, and partner HIV status for the past 4 months. A dichotomous variable was created to identify patients with unsuppressed viral load reporting condomless sex. Any condomless sex with unsuppressed viral load was counted as risk behavior, including those acts with HIV-positive partners, given the risk for HIV reinfection with a second strain ("superinfection") and associated detrimental effects on clinical outcomes including increased viral load and disease progression [55–57].

Data Analysis Plan

Statistical analyses were conducted using R, version 3.5.0 [58].Three logistic regression models, using Firth penalized likelihood method due to separation of binary outcomes, were used to test the association between number of syndemics and: (1) less than 80% ART adherence, (2) unsuppressed viral load (≥ 200 copies/mL), and (3) condomless sex in the context of unsuppressed viral load. All models controlled for age, gender (entered as a dummy variable for cisgender male [vs. cisgender females & gender minorities]), sexual minority status, partnered status (entered as a dummy variable for being in a relationship [vs. those endorsing single, divorced, separated, loss of long term partner, or widowed]), and race/ethnicity (entered as a dummy variable for Black, non-Hispanic/Latinx [vs. everyone else]). For model 2 (outcome = unsuppressed viral load), the model was run in stepwise fashion with the first iteration omitting ART adherence as a covariate, and the second iteration including ART adherence in order to examine the strength of the effect of syndemics on unsuppressed viral load both with and without accounting for adherence. Significant coefficients were transformed and reported in text as odds ratios with 95% confidence intervals. The models were fit using the logistf function in the logistf package (version 1.22).

Results

Sample Characteristics

Table 1 presents patient characteristics. Overall, the sample was a mean of 50 years of age (range 22 to 80), Black,
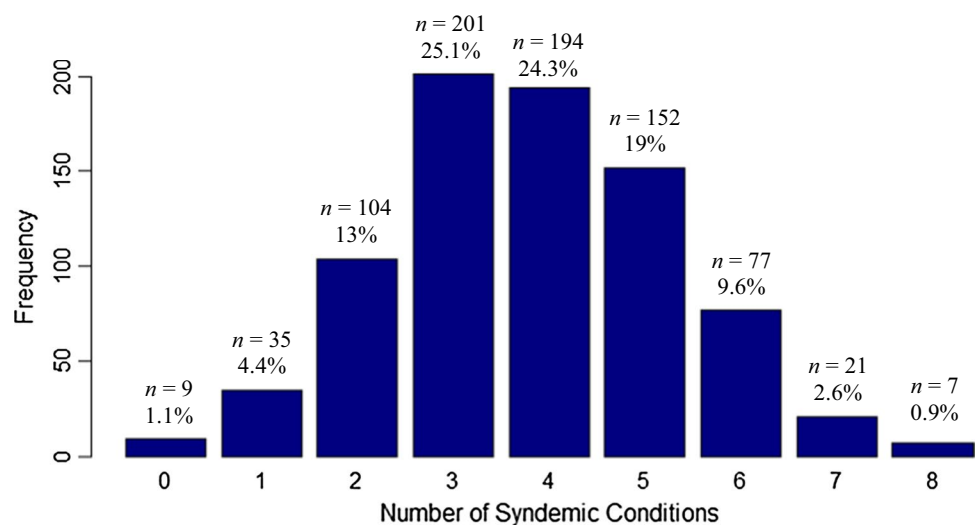
Table 1 Patient characteristics N = 800

	M or *n*	(*SD* or %)	Range
Sociodemographics			
Age	50.2	(11.3)	22–80
Race/ethnicity			
Black, non-Hispanic/Latinx	529	(66.1%)	
Black, Hispanic/Latinx	28	(3.5%)	
White, non-Hispanic/Latinx	32	(4.0%)	
White, Hispanic/Latinx	192	(24.0%)	
Multi, non-Hispanic/Latinx	3	(0.4%)	
Multi, Hispanic/Latinx	6	(0.8%)	
Other, non-Hispanic/Latinx	5	(0.1%)	
Other, Hispanic/Latinx	4	(0.1%)	
Gender			
Cisgender male	450	(56.3%)	
Cisgender female	341	(42.6%)	
Transgender male	1	(0.1%)	
Transgender female	8	(1.0%)	
Sexual orientation			
Straight/heterosexual	609	(76.1%)	
Gay/lesbian/homosexual	126	(15.8%)	
Bisexual	57	(7.1%)	
Different identity	6	(0.8%)	
Relationship status			
Married or living with someone	150	(18.8%)	
Non-cohabitating relationship	46	(5.8%)	
Single	475	(59.4%)	
Divorced or separated	98	(12.3%)	
Loss of long-term partner/widowed	30	(3.8%)	
HIV biomarkers			
Viral load (copies/mL)	10,499.3	(63,056.0)	0–1,066,671
Unsuppressed viral load	143	(17.9%)	
Risk behaviors			
< 80% ART adherence	67	(8.4%)	
Condomless sex in the context of unsuppressed viral load	18	(2.3%)	
Syndemic factors			
1. Unstable housing	146	(18.3%)	
2. Less than high school education	293	(36.6%)	
3. Depression	598	(74.8%)	
4. Anxiety	403	(50.4%)	
5. Drug use	217	(27.1%)	
6. 4 + drinks on drinking day	88	(11.0%)	
7. Violence	686	(85.8%)	
Trauma	596	(74.5%)	
Abuse as a child	373	(46.6%)	
Abuse as an adult	248	(31.0%)	
Relationship abuse	348	(43.5%)	
8. HIV related stigma	616	(77.0%)	

Table 1 (continued)

	M or *n*	(*SD* or %)	Range
Number of syndemic factors endorsed	3.8	(1.5)	0–8

non-Hispanic/Latinx (66%), cisgender male (56%), heterosexual (76%), and single (59%). Patients had an average viral load of 10,499 (range 0 to 1,066,671). Compared to 2018 population estimates for Miami (72% Hispanic/Latinx, 18% Black, non-Hispanic/Latinx, 10% White, non-Hispanic/Latinx) [59], our sample reflects the racial disparities in HIV in Miami. Specifically, despite being 17% of the population of Florida, Black non-Hispanic/Latinx individuals made up 42% of all new HIV diagnoses in Florida [60]; such disparity is reflected in the current sample's proportions (i.e., 66% Black, non-Hispanic/Latinx). The sample had high prevalence of syndemic factors (range 0-8, $M = 3.8$, $SD = 1.5$) including unstable housing (18%), low education (37%), depression (75%), anxiety (50%), drug use (27%), binge drinking (11%), violence (trauma/abuse, 86%), and HIV-related stigma (77%). Figure 1 presents the distribution of syndemic conditions for the sample. Almost the entire sample (99%) experienced 1 + syndemic condition, 95% experienced 2 + conditions, 82% experienced 3 + conditions, 56% experienced 4 + conditions, 32% experienced 5 + conditions, 13% experienced 6 + conditions, 4% experienced 7 conditions, and 1% experienced all 8 syndemic conditions.

Syndemics Predicting Biobehavioral Transmission Risk

Model 1

In examining the association of the number of syndemic conditions with ART adherence, the overall model was significant, $\chi^2(6) = 56.61$, $p < 0.001$. Specifically, each one unit increase in number of syndemic conditions was associated with an expected 64% increase in the odds of having less than 80% ART adherence ($b = 0.49$, SE = 0.09, $\chi^2 = 31.78$, aOR 1.64, 95% CI 1.38, 1.98, $p < 0.001$) while controlling for age, gender, sexual minority status, partner status, and race/ethnicity.

Model 2a

In examining the association of the number of syndemic conditions with unsuppressed viral load, the overall model that did not include ART adherence as a covariate was significant $\chi^2(6) = 55.48$, $p < 0.001$. Specifically, each one unit increase in number of syndemic conditions was associated with an expected 33% increase in the odds of having an unsuppressed viral load ($b = 0.29$, SE = 0.07, $\chi^2 = 19.78$, aOR 1.33, 95% CI 1.17, 1.52, $p < 0.001$) while controlling for age, gender, sexual minority status, partner status, and race/ethnicity.

Model 2b

When including ART adherence as a covariate, the overall model continued to remain significant, $\chi^2(7) = 103.38$, $p < 0.001$. Specifically, each one unit increase in number of syndemic conditions was associated with an expected 16% increase in the odds of having an unsuppressed viral load

Fig. 1 Distribution of number of syndemic conditions

$(b = 0.15,$ SE $= 0.07, \chi^2 = 4.70,$ aOR 1.16, 95% CI 1.01, 1.33, $p = 0.030$) while also controlling for age, gender, sexual minority status, partner status, and race/ethnicity.

Model 3

In examining the association of the number of syndemic conditions with condomless sex in the context of unsuppressed viral load, the overall model indicated a significant association, $\chi^2(6) = 28.48, p < 0.001.$ Specifically, each one unit increase in number of syndemic conditions was associated with an expected 78% increase in the odds of engaging in biobehavioral transmission risk ($b = 0.58,$ SE $= 0.15,$ $\chi^2 = 13.43,$ aOR 1.78, 95% CI 1.30, 2.46, $p < 0.001$) while controlling for age, gender, sexual minority status, partner status, and race/ethnicity. Results from all models are presented in Table 2.

Post-hoc Analysis

In post hoc analyses, we examined if number of syndemic conditions were significantly different among certain subgroups shown to have HIV outcome disparities using independent samples t tests and one-way ANOVA. In examining syndemic distribution among groups, no significant differences emerged between age groups (under 25 years old vs. 25 years +; $t[11.86] = -0.69, p = 0.502$), gender groups (cisgender males vs. cisgender females and gender minorities; $t[798] = -0.29, p = 0.774$), sexual orientations (sexual minorities vs. heterosexual; $t[796] = 0.82,$ $p = 0.414$), or race/ethnicity groups ($F[10, 188] = 0.91,$ $p = 0.527$).

Table 2 Logistic regression models predicting # of syndemics on transmission risk

	b (SE)	χ^2	aOR	95% CI	p
Model 1: < 80% ART adherence $N = 795, \chi^2(6) = 56.61, p < 0.001$					
# of Syndemics	0.49 (0.09)	31.78	1.64	1.38, 1.98	< 0.001
Age	−0.04 (0.01)	9.36	0.97	0.94, 0.99	0.002
Cisgender male	−0.40 (0.27)	2.08	0.67	0.39, 1.15	0.150
Sexual minority	0.31 (0.33)	0.84	1.36	0.69, 2.60	0.360
Partnered	−0.75 (0.39)	4.33	0.47	0.21, 0.96	0.037
Black, non-Hispanic/Latinx	0.71 (0.32)	5.18	2.04	1.10, 3.97	0.023
Model 2a: unsuppressed viral load $N = 772, \chi^2(6) = 55.48, p < 0.001$					
# of Syndemics	0.29 (0.07)	19.78	1.33	1.17, 1.52	< 0.001
Age	−0.04 (0.01)	17.22	0.97	0.95, 0.98	< 0.001
Cisgender male	0.58 (0.21)	8.05	1.78	1.17, 2.67	0.005
Sexual minority	−0.44 (0.26)	2.97	0.64	0.38, 1.06	0.085
Partnered	−0.48 (0.25)	4.07	0.62	0.37, 0.99	0.044
Black, non-Hispanic/Latinx	0.48 (0.23)	4.67	1.61	1.05, 2.54	0.031
Model 2b: unsuppressed viral load $N = 771, \chi^2(7) = 103.38, p < 0.001$					
# of Syndemics	0.15 (0.07)	4.70	1.16	1.01, 1.33	0.030
Age	−0.03 (0.01)	12.25	0.97	0.95, 0.99	< 0.001
Cisgender male	0.70 (0.22)	10.83	2.02	1.33, 3.12	0.001
Sexual minority	−0.52 (0.27)	3.72	0.60	0.35, 1.01	0.053
Partnered	−0.36 (0.25)	2.17	0.70	0.42, 1.12	0.141
Black, non-Hispanic/Latinx	0.32 (0.24)	1.91	1.38	0.87, 2.22	0.167
ART adherence	−0.03 (0.00)	48.07	0.97	0.96, 0.98	< 0.001
Model 3: condomless sex in the context of unsuppressed viral load $N = 793, \chi^2(6) = 28.48, p < 0.001$					
# of Syndemics	0.58 (0.15)	13.43	1.78	1.30, 2.46	< 0.001
Age	−0.07 (0.02)	11.43	0.93	0.90, 0.97	0.001
Cisgender male	0.11 (0.47)	0.05	1.12	0.43, 3.01	0.822
Sexual minority	0.05 (0.58)	0.01	1.05	0.29, 3.23	0.935
Partnered	0.29 (0.55)	0.25	1.34	0.39, 3.84	0.616
Black, non-Hispanic/Latinx	0.97 (0.61)	2.68	2.63	0.84, 10.85	0.102

Discussion

Findings from the present study of people living with HIV/ AIDS in Miami, Florida provided consistent support for the association of greater syndemic burden and ART nonadherence, lower odds of viral suppression, and engagement in biobehavioral HIV transmission risk. In this public HIV clinic in Miami, a domestic epicenter of the HIV epidemic in the U.S., the prevalence of these syndemic conditions was exceptionally high. To date, few studies have examined syndemic theory in the context of persons living with HIV/AIDS, and almost none have been conducted in the Southeast region of the U.S. where HIV rates are disproportionately high compared to other regions of the country. Syndemic theory offers a compelling framework to contextualize Miami's increasing HIV/AIDS epidemic. In the one study conducted in Miami [43], number of individual level barriers to HIV care (e.g., substance use) and number of system level barriers (e.g., transportation) were investigated as separate predictors of viral suppression. Results showed that only individual levels barriers (having 2 + factors) significantly predicted higher odds of detectable viral load. However, as first conceptualized, syndemic theory suggests that both the individual level syndemic factors and the structural level syndemic factors interact to produce worse disease outcomes [13]. Thus, the current study included multiple levels of syndemic conditions within the same syndemic count to examine the combined effects across levels.

Given the findings that intrapersonal (mental health, substance use), interpersonal (violence), societal (stigma), and structural (low education, unstable housing) level syndemic conditions were associated with factors that contribute to HIV transmission, it would be beneficial to explore intervention designs and theories that are able to address the HIV/AIDS epidemic across levels. In considering how to approach an HIV/AIDS epidemic within a complex environment, such as Miami, it is important to explore multilevel, simultaneous interventions. For example, the modified social ecological model [61] posits that individual, interpersonal, community, and public policy levels all influence the course of HIV/AIDS epidemics in specific regions and should be intervened on with a multipronged approach. Notably, the model posits that the stage of the epidemic (i.e., HIV incidence and prevalence) within an individual's network and community determines the risk of disease acquisition. Considering the Southeast's disproportionate rates of HIV, taking this into account may be necessary to reduce HIV incidence. Indeed, examining HIV prevention 25 + years into the epidemic, scholars have brought attention to the notion that employing single level interventions are not sufficient and do not produce substantial nor lasting effects [62, 63]. Although multifaceted interventions are complicated to design and implement, they have the potential to produce large-scale achievements in risk reduction. In conjunction with a multilevel intervention method, promoting a combination of behavioral and biomedical intervention strategies is necessary for maximum impact [64–66] given that HIV acquisition and transmission risk depend on both of these factors.

Although this is among the first known studies to examine how syndemic conditions are associated with HIV outcomes in a city with an HIV/AIDS epidemic, limitations should be noted. Data is cross-sectional, limiting the conclusions of temporality. Given that patients were recruited from a public HIV clinic in Miami, the generalizability is limited and may not reflect individuals connected to other types of care in Miami. However, it should be noted that this is an urban safety-net clinic serving the socially marginalized and underserved individuals not consistently connected to care [43]. There is also increasing recognition that an additive model, depending on a summation of binary variables, may not fully capture the dynamic interplay (e.g., severity of each condition) among syndemic conditions that is theorized to fuel the HIV/AIDS epidemic. Although the current study was able to establish additive effects of syndemic conditions, it did not examine multiplicative relationships as some have argued for as needed following a syndemic framework [67]. However, the current study did not have the sample size to test a fully saturated interaction model with the number of interaction terms that would be required. Further, despite the theoretical strength of potentially examining interaction effects [67], additive models provide practical and clinical significance [68]. The binary outcomes in the current sample had low prevalence; although this was statistically adjusted for in the analysis, this should also be considered a limitation and analysis should be replicated with samples with higher rates. Limitations notwithstanding, findings provide evidence for considering the impact of the occurrence of multiple epidemics happening within the HIV/AIDS epidemic in Miami and other afflicted regions.

Additionally, the sample had representation of important subgroups shown to have disparities in HIV risk and outcomes [69–72] including Black, non-Hispanic/Latinx individuals (66%), Hispanic/Latinx individuals (29%), Black-non-Hispanic/Latinx cisgender women (34%), transgender women (1%), men who have sex with men (21%), and those younger than 25 years old (1.5%). In post hoc analyses, we examined if number of syndemic conditions were significantly different among certain subgroups shown to have HIV outcome disparities. In examining syndemic distribution among age group (under 25 years old vs. 25 years +), gender groups (cisgender males vs. cisgender females and gender minorities), sexual orientations (sexual minorities vs. heterosexual), and race/ethnicities, results showed no

significant differences. Findings may reflect the dire and complex HIV epidemic in Miami such that experiencing multiple psychosocial issues is synonymous with HIV infection. Indeed, 95% of the sample experienced 2 + syndemic conditions. However, it remains important to continuously consider moderated analyses to examine groups with greater HIV disparities in order to appropriately contextualize HIV epidemics in other regions of the U.S.

Despite the unprecedented developments in HIV prevention and care that essentially make HIV a chronic disease, certain geographic areas continue to not fully benefit from such advances. In a region of the U.S. with high HIV incidence and relatively high structural barriers to treatment, the complex syndemic of HIV threatens to undermine the benefits of care and are important in attaining public health HIV treatment goals. Achieving the 90-90-90 UNAIDS targets [73] and the recent U.S. "ending the epidemic" targets [74] will require comprehensive efforts addressing the structural, social, and syndemic determinants of HIV transmission and progression.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee (University of Miami Institutional Review Board; study #20160911) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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