An Index of Multiple Psychosocial, Syndemic Conditions Is Associated with Antiretroviral Medication Adherence Among HIV-Positive Youth

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Abstract

Medication adherence among HIV-infected individuals is critical to limit disease progression and onward transmission. Evidence indicates that among youth living with HIV (YLH), adherence is suboptimal and related to co-morbid psychosocial conditions. Cross-sectional data from 212 YLH, ages 16–29, collected between 2011–2014 in Chicago were analyzed to assess the relationship of multiple psychosocial conditions (e.g., depressive symptoms, anxiety symptoms, moderate/heavy marijuana use, moderate/heavy alcohol use, HIV-related stigma) to ART adherence (i.e., a “syndemic.”) Adherence was regressed on an index of increasing numbers of psychosocial conditions, controlling for demographic and treatment factors as well as enrollment site. The mean age of participants was 24, 89% were male, 87% black, and 91% behaviorally infected. Psychosocial conditions were prevalent, including 38% and 34% with high depressive and anxiety symptoms, respectively, 54% and 25% with a moderate/high level of marijuana and alcohol use, respectively, and 46% reporting high HIV-related stigma. In regression analysis, the likelihood of ART adherence decreased with the number of syndemic conditions (linear dose response, $p=0.02$) as did the odds of viral load suppression ($p=0.008$). Interventions to address these conditions in concert with biomedical treatment as prevention for YLH are needed.

Introduction

ESTIMATES OF RECENT human immunodeficiency virus (HIV) incidence in the United States (US) indicate that over a third of cases occur among young people aged 13–29.¹ The improved life expectancy of individuals living with HIV, largely due to antiretroviral therapy (ART),¹ and the shift to treatment as prevention,² has increased focus on the importance of ART adherence. In patients with HIV, a high level of ART adherence (at least 80%) may be needed to suppress viral replication and avoid resistance;^{3–5} sub-optimal adherence can lead to disease progression and decreased life expectancy for HIV-related disease.^{6–10}

Adolescents and young adults living with HIV, referred to herein as “youth” living with HIV (YLH), are a particularly vulnerable group with regard to medication ad-

herence, as documented in studies dating back more than a decade.^{11,12} Two reviews of ART adherence among youth (aged 12–24 years) suggest low adherence rates, which vary from 30–70% among youth in the United States (in the prior 30 days)¹³ to 46–59% among youth across North America.¹⁴

Correlates of ART adherence among YLH include key psychosocial factors, such as co-morbid depression and anxiety,^{11,15–17} alcohol and drug use,^{11,18} and HIV-related stigma,¹² among other factors.¹³ Furthermore, evidence suggests that the prevalence of these psychosocial conditions is particularly high among YLH,^{18–21} and that they often co-occur and are inter-correlated.^{22,23} The term “syndemic” has been used to describe the clustering of psychosocial and health conditions, including substance use, internalizing mental health problems, and exposure

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to violence and victimization, which may contribute synergistically to poor health outcomes among YLH, particularly in the context of social and economic inequities.²⁴

While the application of syndemic theory to sexual risk for HIV infection, particularly among men who have sex with men (MSM), has been widely studied,^{25–32} only recently has it been applied to ART adherence. In one such study of 333 adults with HIV infection (mean age=47 years; 72% male; 62% white), with adherence measured via electronic pill caps, Blashill and colleagues found evidence to suggest that the odds of non-adherence to ART increased with the number of syndemic conditions (i.e., childhood abuse, current violence, substance abuse/dependence, mental health disorders).³³ Compared to those with no psychosocial conditions, the odds of non-adherence to ART increased monotonically from 4.1 times greater odds in those with 1–2 conditions, to 5.0 greater odds for those with 3–4 conditions, and 8.5 times greater odds for those with 5 or more conditions.³³ These findings may inform clinical practice by helping to identify and intervene on poor adherence among those at greatest risk; however, study findings were limited to an older, mostly white population with HIV infection, and did not include biological outcomes.

The study described herein contributes to the extant literature by assessing the relationship of multiple psychosocial conditions to ART adherence among YLH, a population with low levels of adherence and relatively high rates of co-morbid conditions. In addition, this study employs a biological marker of adherence, viral load, which provides a more objective indicator of adherence as an adjunct to self-reported measures.

Methods

From 2011 to 2014, participants were enrolled in one of two pilot randomized controlled trials at two Chicago locations: one north side and one south side, which tested the efficacy of two separate interventions to improve adherence among YLH, aged 16–29. Both Chicago locations are in or adjacent to neighborhoods with some of the highest HIV incidence and prevalence.³⁴ The north side study took place in neighborhoods that have been at the epicenter of the HIV epidemic in Chicago, whereas the south side study took place in neighborhoods in which HIV incidence has been rising in recent years.³⁴ The north side location tested an intervention to promote adherence to ART medication among poorly adherent YLH (known as TXTXT),³⁵ while the south side location tested a social network-based intervention to promote retention in care among black YLH who also identified as men who have sex with other men (MSM; Project nGage).³⁶ YLH were recruited for each study at community-based health centers and other venues near each location using a direct approach (e.g., in the clinic setting), as well as printed material (e.g., flyers and palm cards).

Individuals were screened for eligibility in person or via telephone. Both studies required that youth be between the ages of 16–29 (inclusive), HIV-positive, have access to or own a cell phone, agree to receive text messages and be English-speaking; however, each targeted a slightly different demographic group. For the south side location,

eligible participants had to be male (birth sex) and report sex with another male in the prior 2 years, identify as black or African American, to be recently diagnosed (past 3 months), and to have at least one supportive person in their social network. In the north side study, there were no eligibility criteria by gender, sexual orientation, or race; however, eligible individuals had to report adherence problems (i.e., missed 1 dose in the past week or ≥ 4 doses in the last month) and regular use of text messaging. Participants received \$25 or \$40 for the baseline visit at the south side and north side locations, respectively. The protocol for each study was approved by each institution's IRB, with a waiver of parental permission for participation of minors.

Data collection and measures

The baseline visit was completed at research facilities in each location. Participants in the north side study completed visits from 2011 to 2013, while enrollees in the south side study completed visits from 2012 to 2014. Participants were screened, scheduled, consented, and enrolled by the study research staff (i.e., research assistants and associates). Baseline measures were collected using computer-assisted administration (both interviewer and self-administration). Whenever possible, we selected measures previously tested in studies of ART adherence, particularly among youth, to maximize comparability to other studies. Measures used in the south side study were synchronized with those used in the north side study (which began earlier) in order to facilitate future analysis of the combined samples.

Demographic variables. Participants were asked their date-of-birth, birth sex, gender identity, sexual orientation, race/ethnicity, highest level of education, employment status, mode of infection, and number of medications and duration on ART (in number of months).

Primary and secondary outcome measures: Medication adherence and viral load. Self-reported adherence was used as the primary outcome, measured using a visual analogue scale (VAS) to rate adherence for each medication taken in the last 30 days on a scale of 0–100%. Among YLH, self-reported measures of adherence have been found to correlate moderately and significantly with viral load,³⁷ including the VAS (i.e., $r = -0.5$).^{38,39} Average adherence was computed to include all ART medications. Viral load was a secondary outcome abstracted from medical records, measured in RNA copies per milliliter, with ≤ 75 copies per mL defined as viral suppression.

Syndemic conditions: Substance abuse, depressive symptoms, and HIV stigma. We measured HIV-related stigma, depressive symptoms, and substance use as components of a syndemic index. Stigma was operationalized with a 10-item scale created and tested for YLH.⁴⁰ A sample item is, “I feel that I’m not as good a person as others because I have HIV.” Responses were provided on a scale of 1-strongly disagree to 5-strongly agree, with higher scores indicating greater stigma. In order to maximize scoring of the stigma scale given missing responses, we computed a scale score for all participants with at least 70% complete items. The stigma scale

was analyzed as both a continuous and binary variable dichotomized about the mean (mean = 2.57).

We measured depressive symptoms with the Brief Symptom Inventory (BSI), a multi-item scale of mental health problems experienced in the last 7 days.⁴¹ A standard cutoff score of ≥ 63 on the depression and anxiety subscales, respectively, were used to indicate high depressive or anxiety symptomology (i.e., 1 vs. 0). Problem alcohol and drug use was assessed with the Alcohol, Smoking and Substance Involvement Screening Test

(ASSIST).⁴² The ASSIST covers 10 substances (in the previous 3 months) and assesses frequency of use and associated problems for each. Dummy variables were created for each substance corresponding to a rating of moderate to high-risk vs low risk (1 vs. 0). The syndemic index (range = 0–5) was computed by summing dichotomous indicators of high vs. low scores (i.e., 1, 0) on the following five indicators: HIV stigma, depressive symptoms, anxiety symptoms, moderate/high alcohol use, and moderate/high marijuana use.

TABLE 1. COMPARISON OF SITES BY DEMOGRAPHIC CHARACTERISTICS

	Total (N=212) n (%) or median (IQR)	North side (N=106) n (%) or median (IQR)	South side (N=106) n (%) or median (IQR)	p Value
<i>Sex at birth</i>				
Male	192 (91.0)	86 (81.9)	106 (100.0)	<0.001
Female	18 (8.5)	18 (17.1)	0 (0.0)	
Intersex	1 (0.5)	1 (0.9)	0 (0.0)	
<i>Gender identity</i>				
Male	188 (89.1)	84 (80.0)	104 (98.1)	<0.001
Female	18 (8.5)	18 (17.1)	0 (0.0)	
Transgender M to F	5 (2.4)	3 (2.9)	2 (1.9)	
<i>Sexual orientation</i>				
MSM/gay/bisexual	181 (86.6)	77 (73.3)	104 (100.0)	<0.001
Heterosexual/straight	26 (12.4)	26 (24.8)	0 (0.0)	
Questioning	2 (1.0)	2 (1.9)	0 (0.0)	
<i>Race/ethnicity</i>				
Black/African-American	184 (87.2)	78 (74.3)	106 (100.0)	<0.001
White	5 (2.4)	5 (4.8)	0 (0.0)	
Latino/Hispanic	8 (3.8)	8 (7.6)	0 (0.0)	
Multi-racial	3 (1.4)	3 (2.9)	0 (0.0)	
Other	11 (5.2)	11 (10.5)	0 (0.0)	
<i>Age, median (IQR)</i>	24.0 (22.0–26.4)	23.7 (22.0–26.4)	24.2 (22.0–26.4)	0.558
<i>Employment</i>				
Working full-time	36 (17.3)	10 (9.5)	26 (25.2)	0.006
Working part-time	66 (31.7)	33 (31.4)	33 (32.0)	
Not employed	106 (51.0)	62 (59.1)	44 (42.7)	
<i>Education</i>				
<HS	34 (16.4)	14 (13.3)	20 (19.4)	0.321
HS/GED	56 (26.9)	25 (23.8)	31 (30.1)	
Some college	89 (42.8)	48 (45.7)	41 (39.8)	
Technical/Associates degree	14 (6.7)	8 (7.6)	6 (5.8)	
Bachelor's degree	12 (5.8)	9 (8.6)	3 (2.9)	
Master's degree or above	3 (1.4)	1 (0.9)	2 (1.9)	
<i>Mode of infection</i>				
Behavioral	192 (91.0)	86 (81.9)	106 (100.0)	<0.001
Perinatal	10 (4.7)	10 (9.5)	0 (0.0)	
Other	9 (4.3)	9 (8.6)	0 (0.0)	
<i># Meds</i>	1 (1–3)	2 (1–3)	1 (1–1)	<0.001
<i>Duration of meds</i>	11.1 (4.2–24.8)	11.1 (5.3–26.4)	11.4 (2.1–23.9)	0.140
<i>Adherence (VAS average) (n=196)</i>	80 (68.3–96.5)	70 (50–90)	96 (80–100)	<0.001
<i>Viral load <75 copies/mL (n=179)</i>	106/179 (59.2)	61/93 (65.6)	45/86 (52.3)	0.071
<i>HIV stigma high, n (%)</i>	87 (46.0)	59 (67.1)	28 (27.7)	<0.001
<i>Anxiety high, n (%)</i>	71 (34.1)	38 (36.2)	33 (32.0)	0.528
T-score, med (IQR)	55 (46–64)	55 (46–57)	55 (48–64)	0.582
<i>Depression high, n (%)</i>	78 (37.5)	45 (42.9)	33 (32.0)	0.107
T-score, med (IQR)	58 (48–67)	61 (50–67)	52 (48–64)	0.008
<i>Alcohol high, n (%)</i>	51 (24.5)	22 (21.0)	29 (28.2)	0.227
<i>Marijuana high, n (%)</i>	113 (54.3)	51 (48.6)	62 (60.2)	0.093

p Value by Chi-Square, Fisher's exact test, or Wilcoxon rank-sum test.

Column totals may not sum to N due to missing data.

TABLE 2. MEDIAN ADHERENCE^a BY EXPOSURE CATEGORIES AND SYNDOMIC COMPONENTS

	n	Adherence median (IQR)	Wilcoxon rank-sum/ Kruskal-Wallis p value
<i>Sex</i>			
Male	177	85 (70–98)	0.006
Female	18	63.3 (30–80)	
Intersex	1	90 (90–90)	
<i>Gender identity</i>			
Male	175	85 (70–98)	0.006
Female	18	63.3 (30–80)	
Transgender M to F	3	90 (80–90)	
<i>Sexual orientation</i>			
MSM/gay/ bisexual	168	88.2 (70–98)	<0.001
Heterosexual/ straight	26	68.3 (40–90)	
Questioning	2	40 (40–40)	
<i>Race/ethnicity</i>			
Black/African- American	169	80 (66.7–98)	0.372
White	5	90 (80–90)	
Latino/Hispanic	8	62.5 (40–85)	
Multi-racial	3	90 (80–90)	
Other	11	80 (70–90)	
<i>Employment</i>			
Working full-time	34	90 (75–100)	0.047
Working part-time	59	80 (60–90)	
Not employed	101	80 (70–95.7)	
<i>Education</i>			
<HS	33	90 (70–96)	0.660
HS/GED	52	80 (60–96)	
Some college	81	80 (70–90)	
Technical/ Associates degree	13	75 (55–97.5)	
Bachelor's degree	12	85 (72.5–90)	
Master's degree or above	3	99 (80–100)	
<i>Mode of infection</i>			
Behavioral	177	85 (70–98)	0.013
Perinatal	10	58.3 (40–70)	
Other	9	75 (50–90)	
<i>HIV stigma</i>			
High	81	80 (60–90)	<0.001
Low	94	90 (75–100)	
<i>Anxiety</i>			
High	69	80 (60–90)	0.035
Low	125	90 (70–98)	
<i>Depression</i>			
High	75	80 (60–95)	0.092
Low	119	85 (70–98)	
<i>Alcohol</i>			
Abuse/dependence	45	80 (60–90)	0.071
Low	149	85 (70–98)	
<i>Marijuana</i>			
Abuse/dependence	103	80 (70–95.7)	0.841
Low	91	83.3 (65–97)	

(continued)

TABLE 2. (CONTINUED)

	n	Adherence median (IQR)	Wilcoxon rank-sum/ Kruskal-Wallis p value
<i>Syndemic index</i>			
0	37	90 (80–100)	0.034
1	47	80 (70–98)	
2	45	85 (70–90)	
3	36	75 (60–96)	
4	17	70 (40–90)	
5	12	80 (65–92.5)	

^aTotal N with adherence data = 196.*Data analysis*

Baseline characteristics between sites and median adherence by demographic characteristics, as well as syndemic conditions, were compared using Chi-square tests for categorical variables and Wilcoxon rank-sum tests or Kruskal-Wallis tests for continuous variables. Correlations between syndemic indicators and level of adherence were computed using Spearman rank order correlations. Unadjusted and adjusted linear regression models were used to examine the association of the syndemic index with adherence, adjusting for site, age, number of medications, and gender identity. Linear regression assumptions were assessed with standard model diagnostics, including graphical examination of residuals and leverage plots and comparison of residuals with predicted values; all of which indicated adequate model fit.

Syndemic index was evaluated as a categorical variable with 0 as the reference category, and tests of linear dose response were evaluated by regressing adherence on the syndemic index as a continuous exposure. While the primary outcome of interest was self-reported adherence to ART (given missing data for viral load), we ran a secondary logistic regression model with viral load suppression (yes vs. no) as the outcome of interest to determine whether the association between the syndemic index was similar using self-reported and biological outcome measures of adherence. Analyses were conducted using SAS software version 9.3 (SAS Institute, Cary, NC).

Results*Descriptive characteristics by site*

Data from 212 study enrollees are analyzed herein (i.e., $n = 106$ north side, $n = 106$ south side). Participants were largely male, in terms of birth sex (91%) and gender identity (89%). The majority identified as gay/bisexual or MSM (87%), and black (87%; see Table 1). The median age was 24 (IQR = 22–26). About half of participants were not employed (51%); however, the vast majority had a high school or greater level of education (84%). In terms of treatment-related factors, 91% of participants were behaviorally infected, with a median number of just one medication and less than 1 year on ART. The level of adherence in the prior 30 days was reported to be 80% on average. Among those with viral load data available ($n = 179/212$), 59% were virally

TABLE 3. SPEARMAN RANK CORRELATIONS BETWEEN SYNDemic INDICATORS AND ADHERENCE, N = 150^a

	<i>HIV stigma</i>	<i>Anxiety</i>	<i>Depression</i>	<i>Alcohol</i>	<i>Marijuana</i>	<i>Adherence</i>	<i>Log₁₀ viral load</i>
HIV stigma	1.0	–	–	–	–	–	–
Anxiety T-score	0.38 ^e	1.0	–	–	–	–	–
Depression T-score	0.47 ^e	0.76 ^e	1.0	–	–	–	–
Alcohol	0.07	0.21 ^d	0.15 ^b	1.0	–	–	–
Marijuana	–0.02	0.18 ^c	0.08	0.08	1.0	–	–
Adherence	–0.31 ^e	–0.22 ^d	–0.26 ^d	–0.09	0.02	1.0	–

^aBased on non-missing observations.^b $p < 0.10$; ^c $p < 0.05$; ^d $p < 0.01$; ^e $p < 0.001$.

suppressed. The prevalence of co-morbid psychosocial conditions was high, with 46% reporting a high level of HIV stigma, 34% and 38% a high level of anxiety and depressive symptoms, respectively, and 25% and 54% reporting moderate/high alcohol and marijuana use, respectively. Given the differing eligibility criteria for each study, there were significant differences in the two sites for sex, gender, sexual orientation, race/ethnicity, mode of infection, number of medications, baseline adherence, and level of stigma.

Adherence by demographic characteristics, exposure categories, and syndemic components

In terms of differences in level of adherence by demographic and treatment categories (Table 2), only sexual orientation and mode of infection were significantly related to adherence with sexual minority youth (i.e., those who identified as MSM, gay, or bisexual in terms of sexual orientation) reporting higher adherence than heterosexual or questioning youth (88% vs. 68% and 40%, respectively, $p < 0.001$) and behaviorally infected youth reporting greater adherence than either perinatally infected youth or those in the “other” category (85% vs. 58% and 75%, respectively, $p = 0.01$). There were significant bivariate differences in levels of adherence by categories of syndemic indicators, including HIV stigma (high = 80%, low = 90%, $p < 0.001$) and anxiety symptoms (high = 80%, low = 90%, $p = 0.035$).

Correlational analysis (Table 3), demonstrated positive and significant correlations between HIV stigma, anxiety and depressive symptoms ($r = 0.38$ – 0.76); between anxiety symptoms and moderate/heavy alcohol and marijuana use ($r = 0.18$ – 0.21); and significant and negative correlations between adherence and HIV stigma, anxiety and depressive

symptoms ($r = 0.22$ – 0.31). Moderate/heavy alcohol and marijuana use were not significantly correlated with HIV stigma, depressive symptoms or level of adherence.

In adjusted regression models (Table 4), an increasing number of syndemic conditions were associated with level of adherence linearly, with the coefficient increasing in strength from -10.5 (95% CI: $-21.6, 0.6$) for those with one condition to -22.0 (95% CI: $-36.7, -7.25$) for those with four conditions, and dropping off to -8.1 (95% CI: $-24.9, 8.6$) for those with five conditions (p value for linear dose response = 0.018), in comparison to those with no psychosocial conditions. Because some psychosocial conditions may be differentially distributed in perinatally vs. behaviorally infected youth,¹⁹ we ran a sensitivity analysis for the final adherence model removing the small number of perinatally infected youth (revised model, $N = 175$) and observed the same pattern of results (p value for linear dose response = 0.017 ; data not shown). In addition, in order to estimate the relationship between the syndemic index and a biomarker of adherence, viral load suppression, we regressed it on increasing numbers of psychosocial conditions ($N = 176$). This model demonstrated a very similar pattern of findings, with lower odds of viral load suppression with increasing numbers of syndemic conditions (p value for linear dose response = 0.008 ; Table 5).

Discussion

This study is the first to assess the relationship of multiple psychosocial conditions to ART adherence among HIV-positive youth. Similar to prior research with adults,³³ we found that multiple conditions have an additive effect on adherence, with increasing numbers of psychosocial conditions decreasing the likelihood of ART adherence. In

TABLE 4. UNADJUSTED AND ADJUSTED ASSOCIATION OF SYNDemic INDEX WITH ADHERENCE, N = 194

	<i>Unadjusted effect estimate (95% CI)</i>	<i>p Value</i>	<i>Adjusted effect estimate^a (95% CI)</i>	<i>p Value</i>
<i>Syndemic index</i>				
0	[Ref]	–	[Ref]	–
1	–10.5 (–21.6, 0.6)	0.063	–8.5 (–18.8, 1.7)	0.103
2	–8.5 (–19.7, 2.65)	0.134	–6.2 (–16.5, 4.2)	0.239
3	–16.2 (–28.0, –4.4)	0.007	–12.9 (–23.9, –1.9)	0.022
4	–22.0 (–36.7, –7.25)	0.004	–20.6 (–34.3, –6.9)	0.003
5	–8.1 (–24.9, 8.6)	0.339	–7.4 (–23.0, 8.2)	0.349
<i>p Value linear dose response</i>	0.014		0.018	

^aAdjusted for site, age, number of meds, and gender.

TABLE 5. UNADJUSTED AND ADJUSTED ASSOCIATION OF SYNDemic INDEX WITH VIRAL LOAD <75 COPIES/ML, N=176

	<i>Unadjusted OR (95% CI)</i>	<i>p Value</i>	<i>Adjusted OR^a (95% CI)</i>	<i>p Value</i>
Syndemic index				
0	1.0 (Ref)	—	1.0 (Ref)	—
1	0.56 (0.21–1.55)	0.265	0.51 (0.18–1.44)	0.205
2	0.47 (0.17–1.30)	0.145	0.47 (0.17–1.33)	0.155
3	0.43 (0.15–1.24)	0.118	0.38 (0.13–1.13)	0.081
4	0.18 (0.05–0.65)	0.009	0.17 (0.04–0.63)	0.008
5	0.28 (0.07–1.16)	0.079	0.26 (0.06–1.13)	0.072
<i>p Value linear dose response</i>	0.009		0.008	

^aAdjusted for site, age, number of meds, and gender.

a secondary analysis with viral load suppression as the outcome of interest, the same pattern was demonstrated with increasing numbers of psychosocial conditions reducing the odds of viral suppression.

These findings have implications for future adherence research and intervention development to address poor adherence among YLH. Tested interventions to improve adherence among YLH are relatively few in number with modest effects.^{13,35,38,43,44} While interventions that focus on primary drivers of poor adherence, such as forgetting to take medication,^{35,43} motivation to take medication,⁴⁴ or providing social support for medication adherence^{38,45} are appropriate for a large percentage of YLH, multi-component and intensive interventions⁴⁶ may be particularly important for those YLH who experience multiple psychosocial barriers to adherence. For example, while both the north and south side studies have shown evidence of efficacy,^{35,36} and in particular, across co-morbid conditions in the north side study,³⁵ the durability of effects may be impacted by combined psychosocial factors.

In the north side study, analysis of adherence trends over the entire 12-month period of observation in the intervention group (i.e., 6-months post-intervention) demonstrated that the adherence trajectory was modified by a combination of moderate/high marijuana use and high depressive symptoms, suggesting that the intervention effect in this group (32% of the intervention arm) diminished over time.³⁵ Thus, a minority of individuals may benefit from multicomponent interventions, particularly in support of durable effects. Screening for these conditions among youth with chronically poor adherence and addressing these conditions in tandem may provide greater efficacy to improve adherence and viral load suppression, leading to both improved health outcomes and limiting onward transmission.

Study findings should be considered in light of the limitations. The study sample was majority black, male, and behaviorally infected (i.e., primarily young men infected through sex with other men) and recruited in an urban environment, thus findings may not translate to other geographic areas and risk groups. However, these demographics are reflective of the majority of new HIV cases identified in the United States, and a concerted focus on improving adherence among black MSM in particular has the potential to impact onward transmission. We did not include a measure of childhood sexual abuse or physical victimization in our study, which have often been used to operationalize exposure to violence as part

of a syndemic of health-related risk, particularly among MSM. HIV stigma was included in lieu of these measures to reflect day-to-day discrimination and poor treatment experienced by many YLH. We found that HIV stigma was, in fact, related to symptoms of anxiety and depression, as well as adherence; however, it may not fully reflect the violence and victimization experienced by many YLH. Thus, our findings may underestimate the effects of multiple psychosocial conditions on adherence.

Overall, this study reflects important findings about the compound nature of psychosocial problems and their relationship to adherence among YLH. Findings highlight the importance of health care providers attending to and providing social support and counseling for the mental health, substance use, and HIV-related stigma concerns of YLH given their cumulative relationship to ART adherence. Interventions to address these conditions in concert with biomedical treatment as prevention for YLH are needed, especially given the dearth of tested interventions for this population, including those with multiple components.

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