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EFFECTS OF SYNDEMICS ON HIV VIRAL LOAD AND MEDICATION ADHERENCE IN THE MULTICENTER AIDS COHORT STUDY

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Abstract

OBJECTIVES—To determine associations between intertwining epidemics (syndemics) and HIV medication adherence and viral load levels among HIV-positive men who have sex with men (MSM); and to test whether adherence mediates the relationship between syndemics and viral load.

DESIGN—We analyzed participant data collected between 2003—2009 from the Multicenter AIDS Cohort Study, a prospective HIV/AIDS cohort study in four U.S. cities.

METHODS—We conducted longitudinal analyses (repeated measures mixed models) to assess if differences in viral load levels, undetectable viral load, and self-reported HIV medication adherence were associated with count of syndemic conditions (substance use, depression symptoms, and sexual risk behavior, range 0 to 3), adjusting for race/ethnicity, age, and income. Mediation analyses were conducted using structural equation modeling and the SAS %mediate macro.

RESULTS—Syndemics count was associated with higher viral loads (p<.0001) and lower adherence (p<.0001). Increased counts of concomitant syndemics were associated with viral load (p <.01), detectable viral load (p <.05), and adherence (p <.001). Black MSM experienced worse outcomes across domains than White MSM (p <.0001) and experienced higher overall rates of syndemics (p<.01). Adherence significantly mediated the relationship between syndemics and viral load, accounting for an estimated 32.3% of the effect (p<.05).

CONCLUSIONS—Effectively lowering viral load levels among MSM has implications for both HIV/AIDS prevention and care. Our findings suggest that integrating substance use interventions, mental health care, and sexual risk prevention into standard HIV care may be necessary to optimize treatment and Treatment as Prevention (TasP) models.

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AUTHOR CONTRIBUTIONS

MRF, RS, CW, MP, and AJS designed the analysis. MRF led the manuscript writing, to which RS, SW, MP, AJS, SS, PJS, and LT contributed. MRF, AH, and MP collaborated on post-hoc analyses and manuscript revisions.

Keywords

HIV/AIDS; antiretroviral therapy; drug users; viral load; sexual behavior; psychosocial factors; men who have sex with men

INTRODUCTION

Men who have sex with men (MSM) accounted for 65% of new HIV diagnoses in the U.S. in 2013 [1]. HIV incidence rates have been estimated at 2.4% annually for MSM [2]. Among all risk groups, HIV incidence is increasing most sharply among younger MSM, especially African Americans [3]. High background HIV prevalence has been theorized to explain HIV incidence disparities among and within MSM [4-6]. Populations hosting high background HIV prevalence rates experience greater likelihoods for new HIV infections, as each sexual act involves a higher probability of involving a partner with HIV viremia sufficient for transmission. Efforts to reduce viremia among HIV-positive individuals underpin the HIV care continuum, which delineates the proportions of people living with HIV in the U.S. who are aware of their status (80%); linked to care (62%); retained in care (41%); receive antiretroviral therapy (ART) (36%); and have undetectable viral load (28%) [7]. Reducing HIV incidence among MSM requires that HIV-positive MSM are assisted in achieving undetectable viral loads [8, 9]. Now more than 15 years into the ART era, we have yet to reach this goal nationwide. This suggests that there are significant barriers preventing HIV-positive MSM from achieving undetectable viral loads.

Syndemics Theory as applied to MSM posits that MSM experience a set of synergistic epidemics that combine to amplify HIV risk, acquisition and transmission. According to Syndemics Theory, early life adversities, such as violence victimization, faced by MSM are associated with psychosocial conditions, including depression and substance use, in young adulthood, which in turn influence sexual risk behavior that, coupled with high background HIV prevalence, leads to high HIV incidence rates and other health disparities in adulthood [10-20]. Recent research has demonstrated robust associations between early social adversities such as childhood abuses and syndemic production in adulthood among MSM [11]. While the concept was developed largely using samples of dominant culture MSM, syndemic effects have also been measured among Black MSM [12]. Higher rates of independent syndemic variables, for example stimulant drug use, have been linked to HIV sero-conversions among MSM [21]. Substance use, especially stimulants, has also been associated with increased viral replication [22, 23], higher viral load levels [24], and lower ART adherence [25] among HIV-positive MSM, though consistent ART adherence among stimulant users has been shown to swamp stimulants' measured negative immune effects [26]. Depression has been associated with lower adherence and poor HIV treatment outcomes [27-29]. However, few studies have attempted to test the additive and collective effects of syndemics on ART adherence and viral load suppression; and little research has been done analyzing these effects longitudinally.

To respond to this gap in the literature, we assessed the longitudinal associations of syndemics on adherence and viral load among HIV-positive MSM. Specifically, we asked

the following three research questions. First, is higher syndemics count (the number of syndemic conditions experienced concomitantly) associated with weaker viral load suppression? Second, are higher syndemics counts associated with lower ART adherence? Finally, does adherence mediate the relationship between syndemics count and viral load? To answer these questions, we analyzed biological, psychosocial, and behavioral data over a period of seven years, using a sample of sexually active, HIV-positive MSM participating in the Multicenter AIDS Cohort Study (MACS).

METHODS

Sample

A longstanding observational cohort study of the natural and treated history of HIV/AIDS among MSM in the U.S., the MACS began enrollment in 1984, recruiting successive cohorts in Los Angeles, Pittsburgh, Chicago, and Baltimore. Descriptions of recruitment strategies and research design can be found elsewhere [30, 31]. Every six months, MACS participants complete behavioral and medical surveys, neuropsychological and physical examinations, and collection of blood and other specimens. All MACS participants were offered a supplemental survey, the Methamphetamine Sub-Study, in 2008-2009, corresponding to study visits (waves) 49 and 50; this survey collected data about life-course characteristics theorized to be associated with heightened HIV behavioral risk. The present analysis considered psychosocial, behavioral, and biomedical measures from the 766 MSM who were either HIV-positive at wave 38 (2003-2004) or who sero-converted by wave 50; who reported sexual activity with men during this span; and who were offered the Methamphetamine Sub-Study in waves 49/50. A subset of 712 of these men reporting ART use during this span was included in adherence-related analyses.

Measures

Sociodemographics—Measures for sociodemographic covariates (income, race/ethnicity, bisexual behavior, and recent sero-conversion) have been described elsewhere [11, 32].

HIV viral load—Measured using the COBAS Ultrasensitive Amplicor HIV-1 monitor assay for HIV RNA (Roche Molecular Systems, Branchburg, NJ), sensitive to 50 copies HIV RNA/mL^3. We used a dichotomous variable to denote undetectable (<50 copies/mL^3) vs. detectable HIV viral load for binary outcomes; and $\log_{10}$-transformed viral load values for continuous outcomes.

ART adherence—Assessed using an adherence scale measuring four levels of self-reported adherence since last visit, which has been described elsewhere [28, 33].

Depression symptoms—Assessed at each visit using the Center for Epidemiologic Study of Depression symptom checklist. We created a dichotomous variable assessing whether participants had a score ≥16, a cut-off point associated with depression symptoms [34, 35].

Polysubstance use—Using audio computer-assisted self-interviewing (ACASI), participants reported frequency of using each of the following per visit: crack cocaine, powder cocaine, marijuana, ecstasy, heroin, methamphetamines, and other street or club drugs. Longitudinal dichotomous variables were computed assessing whether participants reported using ≥2 of these substances at least monthly.

Condomless anal sex with casual male partner(s)—Men were asked to distinguish insertive and receptive anal sex behaviors with casual male partners from those behaviors with main male partners. Dichotomous variables were created that corresponded to any condomless anal sex with casual male partners per visit (referred to as "UAI", for unprotected anal intercourse).

Syndemics count—The sum (0-3) per subject, by visit, of the number of syndemic conditions experienced (depression symptoms, polysubstance use, and UAI); treated as a continuous variable.

Statistical analysis

To test for longitudinal effects of syndemics on viral load and ART adherence, we conducted a series of generalized linear mixed models (SAS PROC GLIMMIX), using a repeated measures statement to control for within-subject variance across time and a distribution statement (e.g., binary for dichotomous outcome variables; gamma for right-skewed continuous variables) with corresponding log-link specifying appropriate distributions. Covariance matrices were derived from each model's variance components. Least-squares means were estimated using observed margins for independent variable groups; within-group analyses were conducted by level (to estimate additive effects) and further adjusted using the studentized maximum modular approach to minimize error rates associated with heteroscedasticity and subgroup multiplicity (e.g., outcomes within race/ethnicity groups and additive effects by syndemics count). Trajectory effects of syndemics count on viral load over time were included in these models, estimated using a predictor X time statement (e.g., syndemics count*wave). In post-hoc analyses, we used the statistical approaches described above to test associations between syndemics count and race/ethnicity subgroups; and to assess the interrelatedness of variables comprising syndemics count.

Mediation analyses were conducted to test relationships between syndemics count, ART adherence, and viral load. We hypothesized that the relationship between syndemics count and $\log_{10}$ viral load was mediated by adherence in MSM who reported using ART. We used a structural equation modelling (SEM) approach using STATA 13.0 that estimated the total, direct and indirect effects of the relationships between syndemics count, ART adherence, and viral load. SEM analyses utilized a cross-lagged panel model, operationalizing "since last visit" measures of adherence and syndemics count as "lagged" measures for each visit's contemporaneous viral load measure, controlling for participants' prior reported values of syndemics count, adherence, and viral load [36]. Then, we estimated the percentage of the longitudinal mediated effect of adherence on the relationship between syndemics count and viral load, using the publicly available SAS macro, %mediate (http://www.hsph.harvard.edu/faculty/spiegelman/mediate.html)[37]. All models were adjusted for

race/ethnicity; annual income<$20,000; recent sero-conversion; bisexual behavior; age<40; and wave. We reported overall fixed effects *p*-values and least-squares means estimates for outcomes of interest, as well as F-statistics across group classifications (collective effects) for continuous outcomes.

RESULTS

Sociodemographics

Table 1 shows that of the 766 HIV-positive, sexually-active MSM in this sample, 57.8% identified as non-Hispanic White; 7.3% as Hispanic White; 26.8% as Black; 6% as other Hispanic; and 1% as Hispanic Black. The vast majority (86.2%) were over 40, with 11.5% between 30 and 39, and 2.3% between 20 and 29. 42.7% were recruited in the first cohort (1984); 10.1% in the second cohort (1987); and 47.3% in the most recent cohort (2002). Participants were similarly represented in Baltimore (23.1%), Chicago (23.0%), and Pittsburgh (21.9%), with Los Angeles most represented (32.0%). 6.3% reported bisexual behavior between waves 38-50 while 93.7% had sex only with men.

ART adherence

Table 2 shows that overall, syndemics count was significantly associated with reported ART adherence (F=37.75, $p<.0001$), though trajectories of adherence were not associated with syndemics count (F=0.94, $p=0.57$). Racial/ethnic minority status (F=42.58, $p<.0001$) and low income (F=16.39, $p<.0001$) were associated with adherence levels. Table 3 shows that syndemics count has a by-level effect on adherence, with one syndemic condition significantly predictive of lower adherence ($p<.0001$) compared to no syndemic conditions; two syndemic conditions significantly predictive of lower adherence compared with one syndemic condition ($p<.0001$); and three syndemic conditions significantly predictive of lower adherence compared with two syndemic conditions ($p<.001$). Black MSM ($p<.0001$), Hispanic MSM ($p<.001$), and MSM of other race/ethnicities ($p<.05$) reported lower ART adherence than White MSM.

HIV viral load

Table 2 shows that syndemics count was highly associated with HIV viral load (F=11.39, $p<.0001$), along with bisexual behavior (F=5.52, $p<.05$), wave (F=2.05, $p<.05$), racial/ethnic minority status (F=67.75, $p<.0001$), lower income (F=64.04, $p<.0001$), younger age (F=57.58, $p<.0001$), and recent sero-conversion (F=69.50, $p<.0001$). While viral load levels decreased over time (F=2.05, $p<.05$), trajectories were not associated with syndemics count (F=1.01, $p=0.45$). Table 3 shows that syndemics count has an increasing effect on HIV viral load least-squares means, by level, at a given observation. One syndemic condition (247.69 copies/mL^3) was significantly predictive of higher viral load values ($p<.001$) compared with no syndemic conditions (191.34 copies/mL^3); two syndemic conditions (376.44 copies/mL^3) significantly predicted ($p<.001$) higher viral load values compared with one syndemic condition; and three syndemic conditions (1197.02 copies/mL^3) significantly predicted higher viral load values compared with two syndemic conditions ($p<.01$). Black and Hispanic MSM had significantly higher viral load levels at a given observation than White

MSM (635.04 copies/mL^3 vs. 247.86 copies/mL vs. 153.43 copies/mL^3, respectively; $p <$. 0001).

Proportion of sample with detectable virus

Table 2 shows that the proportion of HIV-positive MSM who had detectable viral loads was associated with syndemics count (F=8.56, p<.0001). The proportion of this sample with detectable viral loads decreased significantly over time (F=3.47, p<.0001); trajectories of this decrease were not significantly different by syndemics count (F=0.86, p=.70), as illustrated in Fig. 2. Table 3 shows that, at a given observation, the likelihood (least-squares means estimated proportions) of having detectable viral load increased with syndemics count. MSM with no syndemic conditions were less likely to have detectable virus than MSM with one syndemic condition (33.5% vs. 38.3%; p<.001); MSM with two syndemic conditions were more likely than MSM with one syndemic condition to have detectable virus (44.5% vs. 38.3%; p<.05); and MSM with three syndemic conditions were more likely to have detectable virus than MSM with two syndemic conditions (65.8% vs. 44.5%; p<.01). Relative to White MSM, Black MSM (57.0% vs. 29.0%; p<.0001) and Hispanic MSM (35.4% vs. 29.0%; p<.01) were significantly more likely to have detectable viral loads. Bisexually-behaving MSM were more likely to have detectable viral load than other MSM (43.9% vs. 36.7%; p<.01); younger MSM were more likely to have detectable viral load than MSM age 40 and older (49.6% vs. 35.4%; p<.0001); lower income MSM were more likely to have detectable viral load than higher income MSM (44.2% vs. 33.3; p<.0001); and recent sero-converters had greater likelihood of detectable viral load (83.1% vs. 36.7%, p<. 0001).

Syndemics count by socio-demographic characteristics

Table 2 shows that, of sociodemographic covariate classes, only lower income status was associated with syndemics count (p<.0001); syndemics count did not change significantly over time (F=0.98, p=.47). Table 3 shows that, within race/ethnicity classifications, Black MSM experienced higher estimated means of syndemics count compared to White MSM (1.30 vs. 1.24; p<.01) at a given observation.

Mediation analyses

Figure 1 shows that, at each study visit assessed, higher syndemics count was associated with lower ART adherence (all p-values<.01) and that, in 10 of 13 visits, lower adherence was significantly associated with higher HIV viral load. In 9 of 13 visits, syndemics count was significantly associated with higher HIV viral load; and in 11 of 13 visits, there was a significant indirect (mediating) effect of adherence on the relationship between syndemics count and HIV viral load. Table 4 shows that the overall mediating effect of adherence on this relationship across visits was significant, estimated to be 32.3% (95% CI: 5.3%--59.2%; p<.05). Nonetheless, even in an adherence-adjusted model, syndemics count was significantly and positively associated with HIV viral load (β=0.03, p<.05).

Interrelatedness of syndemics count variables

Table 5 shows that, longitudinally and adjusting for covariates, polysubstance use was significantly correlated with depression symptoms (F=34.19, $p<.0001$) and UAI (F=69.76, $p<.0001$); depression symptoms were significantly correlated with polysubstance use (F=32.41, $p<.0001$) and UAI (F=25.14, $p<.0001$); and UAI was significantly associated with polysubstance use (F=66.57, $p<.0001$) and depression symptoms (F=24.44, $p<.0001$).

DISCUSSION

Our findings provide robust evidence that, within this sample of HIV-positive MSM, higher HIV viral load and lower ART adherence are, respectively, associated with increased syndemics count. These findings indicate that combinations of depression symptoms, polysubstance use, and sexual risk behavior function as profound barriers to fully reaping the benefits of successful HIV care and that, as these conditions snowball, their impact on HIV outcomes is exacerbated. These results may have epidemiological implications: every increase in the number of concomitant syndemics is associated with higher HIV viral load and, therefore, higher transmission potential. Our finding that adherence significantly but incompletely mediates the effect of syndemics on viral load suggests that the pathway to consistent viral suppression is, for many individuals, complex, and that the concomitant effects of polysubstance use, depression symptoms, and risky sexual behavior may play a role above and beyond their association with ART adherence. It is possible that this finding, in particular, is an artifact of the potential reliability and validity errors associated with our ART adherence measure; or that MSM who are depressed, use illegal substances, and/or have risky sexual behavior are more predisposed to social desirability bias or poorer recall when responding to adherence questions. Other factors we were unable to assess, such as lower retention in care and inconsistent ART regimen monitoring, may occur more frequently among MSM with higher syndemics counts. It is also possible that some latent biological effect exists: other research has shown that methamphetamine and other stimulant drug use may increase viral replication and/or have immunological effects on viral suppression [24, 38]. In the larger context of HIV viral load suppression, these findings suggest that solely biomedical interventions may be less than sufficient for optimal treatment, especially within the newly predominant Treatment as Prevention (TasP) model [39]. Our findings provide support for integrating structural and behavioral approaches to address syndemics among MSM receiving HIV care in the U.S.

These results also contribute to establishing the relevance of Syndemics Theory for MSM, adding additional behavioral (adherence) and biomedical (viral load suppression) endpoints to the model and providing empirical evidence of syndemics' predictive properties in association with HIV outcomes. Syndemics have been repeatedly shown to correspond with HIV risk behavior among HIV-negative MSM; we now see that syndemics impact HIV treatment outcomes among HIV-positive MSM. In addition, our findings support the concept of syndemics as closely intertwined psychosocial conditions whose overall effect on health increases at each level of their combination.

It is of particular concern that men who have sex with men and women (MSMW) and racial/ethnic minority MSM experience higher levels of viral load even in models that control for

syndemics. HIV-positive MSMW were not found to experience higher syndemics count or lower ART adherence in these models; however, it is possible that their small sample size (n=48) limited our ability to identify distinctions: previous research has indicated that MSMW report disparate levels of depression symptoms and polysubstance use compared with other MSM [32, 40]. Our findings on disparities among HIV-positive racial/ethnic minority MSM, especially Black MSM, are very stark: compared with White MSM, they had higher viral loads; higher rates of detectable viral loads; reported lower ART adherence; and reported higher syndemics counts. This suggests that health care systems must be more attentive to possibilities of treatment failure among HIV-positive racial/ethnic minority MSM above and beyond standard intervention approaches, providing further support for recommendations to develop structural interventions designed to assist HIV-positive Black MSM in managing the pressures of dual identities and familial and social stressors [12].

The current battery of HIV interventions aimed at MSM, many of which focus on substance use or depression or sexual risk, often in exclusion, have been shown to have minimal if any long-term benefit [41]. Our findings suggest that a TasP approach that factors in the syndemic array of psychosocial and behavioral conditions and the social adversities that promote them may be more salient for MSM, indicating a need for a continuum-of-care approach to HIV care among MSM, one that includes regular mental health and substance use screenings and treatment, and sexual risk prevention to reduce rates of secondary transmission and acquisition of other STIs [42-44]. Models that also provide ancillary services, for example dedicated housing for active substance-using HIV-positive MSM or those of lower socio-economic status, have been shown to positively impact viral load suppression [45]. If applied across HIV treatment cascade levels such as linkage to and retention in care, a continuum-of-care “best-practices” model should facilitate optimal HIV treatment results by attending to these psychosocial factors so strongly associated with both poor adherence and biomedical outcomes.

This study has several important limitations. First, while the MACS provides an opportunity to analyze viral load suppression, ART adherence, and syndemics over time, the sample is over-represented by older MSM; as such, findings may not be generalizable to younger samples, where risk of HIV infection is highest [3]. Second, men who agreed to participate in the Methamphetamine Sub-Study may have important differences from men who declined to participate, and thus may not be generalizable to the larger MACS sample. As is the case with many cohort studies, measures were subject to missing data from incomplete sections or skipped visits. We were only able to include three longitudinally measured syndemic conditions; other conditions that were not measured longitudinally, such as sexual compulsivity [46], transactional sex engagement [40, 47], and intimate partner violence [11] might provide more comprehensive syndemics measures. Other studies have indicated that measures we have used, such as self-reported adherence, are subject to recall and response biases [48]. However, the robustness of our findings using conservative statistical models and a model subject population (who, as a result of their participation, obtain free lab values every six months, as well as linkage to care beyond research study confines), indicate that our results may well underestimate the variance in adherence and viral load suppression contributed by syndemics in the larger population of sexually active, HIV-positive MSM in the U.S.

In the fourth decade of the U.S. HIV/AIDS epidemic, we remain challenged at a population level by rising HIV incidence rates among MSM and fractional treatment success . The findings we have presented demonstrate that the TasP model will only succeed if it includes a combination of prevention approaches. Reliance on pharmacology alone will be as unsuccessful as relying solely on behavioral or structural strategies alone: a bottle of pills, no matter their efficacy, will be ineffective given the near-perfect adherence that practitioners expect from populations who continue to experience profound psychosocial barriers. We strongly recommend the diffusion of HIV clinical care models that provide highly connected, preferably internally delivered mental health, sexual risk behavior prevention, and substance use treatment to optimize viral load suppression among HIV-positive MSM.

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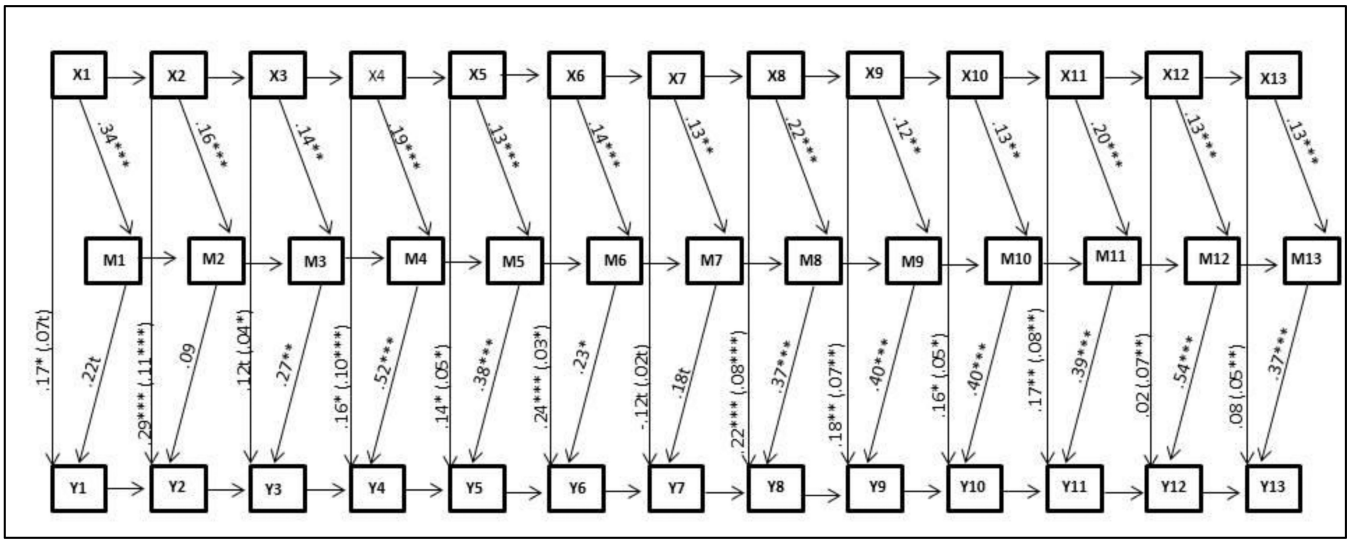

*Where X=Syndemics count (0-3); M=Adherence (1-4); and Y=log$_{10}$ HIV viral load. Numbers 1-13 correspond with observed MACS study visits (waves 38-50). Beta coefficients for total effects are presented, with beta coefficients for indirect effects represented in parentheses. *=p<.05; **=p<.01; ***=p<.001; t=p<.10. Values for within-variable path effects for X, M, and Y (e.g., X1-X2…X13 paths) and standard errors per each assessed variable have been suppressed for readability.*

Figure 1.

Modified cross-lagged panel model (CLPM) with total and indirect effects between syndemics count, HIV medication adherence, and log$_{10}$ viral load in the Multicenter AIDS Cohort Study, visits 38-50 (n=712).

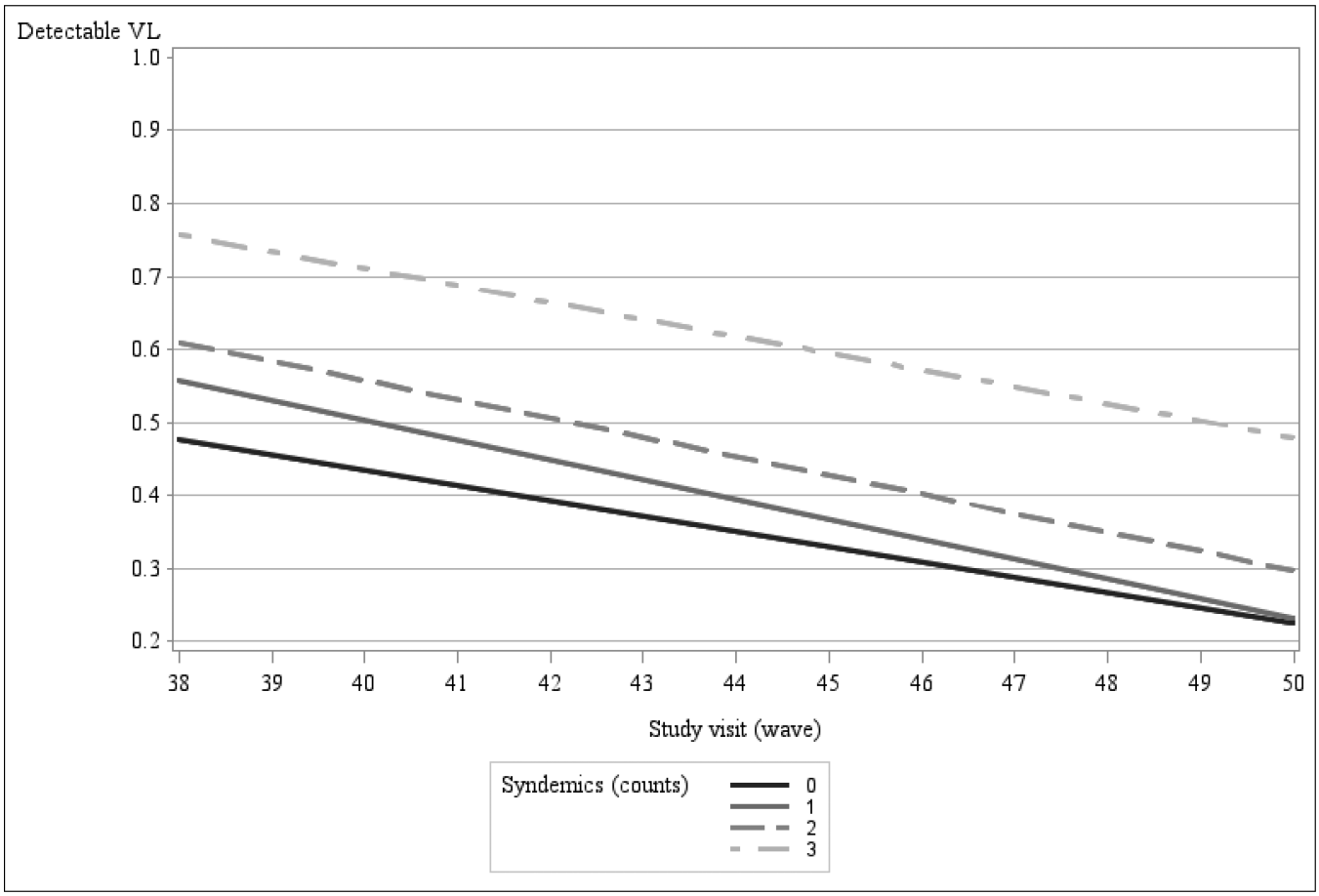

Figure 2.

Regressed least-squares means proportions of HIV-positive MSM with detectable HIV viral load by syndemics count, waves 38-50.

Table 1

Sociodemographics of sexually active HIV-positive MSM in the MACS, wave 50 (n=766)

Sociodemographics	Subcategory	N (%)
Race/ethnicity		
	White, Hispanic	56 (7.3%)
	White, non-Hispanic	443 (57.8%)
	Black, non-Hispanic	205 (26.8%)
	Black, Hispanic	8 (1.0%)
	American Indian or Alaskan	1 (0.1%)
	Asian or Pacific Islander	0 (0%)
	Other	7 (0.9%)
	Other Hispanic	46 (6.0%)
MACS site		
	Baltimore	177 (23.1%)
	Chicago	176 (23.0%)
	Pittsburgh	168 (21.9%)
	Los Angeles	245 (32.0%)
Cohort		
	1984	327 (42.7%)
	1987	77 (10.1%)
	2002	362 (47.3%)
Age		
	20-29	18 (2.3%)
	30-39	88 (11.5%)
	40-49	271 (35.4%)
	50-59	299 (39.0%)
	60+	90 (11.7%)
Income		
	<$10,000	144 (18.8%)
	$10,000-$19,999	123 (16.1%)
	$20,000-$29,999	86 (11.2%)
	$30,000-$39,999	65 (8.5%)
	$40,000-$49,999	57 (7.4%)
	$50,000-$59,999	57 (7.4%)
	$60,000 or more	189 (24.7%)
	No response	45 (5.9%)
Education		
	8^{th} grade or less	9 (1.2%)
	9^{th}, 10^{th}, 11^{th} grade	32 (4.2%)
	12^{th} grade/HS degree	96 (12.5%)
	Some college, no degree	210 (27.4%)
	College degree	140 (18.3%)

Sociodemographics	Subcategory	N (%)
	Some graduate work	72 (9.4%)
	Graduate degree	145 (18.9%)
	No response	62 (8.1%)
Sexual behavior (waves 38-50)		
	MSMO	718 (93.7%)
	MSMW	48 (6.3%)

Table 2

Analysis results of outcomes in the MACS, sexually active HIV-positive MSM, wave 38-50 (n=766)

Predictor variables	**HIV viral load**		**Detectable viral load (%)**		**Adherence scale, since last visit**		**Syndemics count**	
	F-value	***P***	**F-value**	***P***	**F-value**	***P***	**F-value**	***P***
Wave	2.05	0.0170	3.47	<.0001	0.55	0.8810	0.98	0.4691
MSMW	5.52	0.0189	7.69	0.0056	1.12	0.2900	2.00	0.1579
Race/ethnicity	67.75	<.0001	83.88	<.0001	42.58	<.0001	1.33	0.2640
Income < $20,000	64.04	<.0001	61.67	<.0001	16.39	<.0001	23.50	<.0001
Age < 40	57.58	<.0001	54.37	<.0001	0.05	0.8273	0.11	0.7368
Recent seroconverter	69.50	<.0001	51.23	<.0001	2.82	0.0933	0.41	0.5226
Syndemics count	11.39	<.0001	8.56	<.0001	37.75	<.0001	-	-
Syndemics count*Wave	1.01	0.4461	0.86	0.7022	0.94	0.5739	-	-

Table 3

Least-square means group comparisons of viral load and adherence by syndemics count groups (n=766 for all columns, except adherence count, where n=712)

Predictor variables	HIV viral load†‡	Detectable viral load (%)†	Adherence scale (1-4)†	Syndemics count†
Black, non-Hispanic	635.04 copies/mL****	57.0%****	1.9768****	1.2978**
Hispanic	247.86 copies/mL****	35.4%**	1.7550***	1.2849
Other	146.89 copies/mL	27.9%	1.8832*	1.1288
White, non-Hispanic	153.43 copies/mL	29.0%	1.6589	1.2423
MSMW	314.56 copies/mL*	43.9%**	1.8051	1.3031
MSMO	231.10 copies/mL	36.7%	1.7578	1.2950
Recent seroconverter	5468.90 copies/mL****	83.1%****	1.5165	1.3046
Non-recent seroconverter	229.46 copies/mL	36.7%	1.7637	1.2613
Age<40	460.57 copies/mL****	49.6%****	1.7681	1.2550
Age 40 and older	214.34 copies/mL	35.4%	1.7597	1.2628
Income <$20,000	343.95 copies/mL****	44.2%****	1.8140****	1.3163****
Income≥$20,000	190.94 copies/mL	33.3%	1.7304	1.2309
Syndemics count=0	191.34 copies/mL	33.5%	1.6649	-
Syndemics count=1	247.69 copies/mL***	38.3%***	1.7981****	-
Syndemics count=2	376.44 copies/mL***	44.5%*	1.9444****	-
Syndemics count=3	1197.02 copies/mL**	65.8%**	2.3859***	-

†All means adjusted for racial/ethnic minority status, annual income < $20,000, age <40, wave, MSMW status, and recent seroconversion. Least-square means estimate comparisons by syndemic count adjusted for multiplicity and heteroscedasticity using the studentized maximum modular (SMM) approach, using observed margins for means estimates with a by-level estimation approach for multiple comparisons. Significance values for syndemics count are compared to preceding category variable. Significance values for race/ethnicity are compared with white race.

‡HIV viral loads re-transformed post-analysis from $\log_{10}$ values.

*P-value <.05.

**P-value <.01.

***P-value <.001.

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**** P-value <.0001.

Table 4

Mediation of relationship between syndemics count and HIV viral load by HIV medication adherence (n=712)

Viral load (log10)					
Predictors and covariates	**Base model**		**Adherence-adjusted model**		
	β (SE β)	***p***	**β (SE β)**	***p***	**Proportion of effect mediated by adherence % (*p*)**
Syndemics count	0.05 (0.01)	**0.0007**	0.03 (0.02)	**0.03**	**32.3% (.02)**
HIV medication adherence	--	--	0.08 (0.02)	**<0.0001**	--
MSMW	0.13 (0.06)	**0.048**	0.12 (0.06)	**0.049**	--
Minority race/ethnicity	0.09 (0.03)	**0.0009**	0.10 (0.03)	**0.004**	--
Annual income <$20,000	0.12 (0.03)	**<0.0001**	0.10 (0.03)	**0.0008**	--
Recent seroconversion	0.06 (0.07)	0.41	0.21 (0.07)	**0.005**	--

Table 5

Analysis results of syndemic components in the MACS, sexually active HIV-positive MSM, wave 38-50 (n=766)

Predictor variables	**Polysubstance use**		**CES-D>15**		**Condomless anal sex**	
	F	***p-value***	**F**	***p-value***	**F**	***p-value***
Wave	2.04	**0.0174**	1.24	0.2454	0.49	0.9214
MSMW	12.07	**0.0005**	1.54	0.2152	0.25	0.6187
Minority race/ethnicity	2.55	0.1102	11.98	**0.0005**	34.83	**<.0001**
Income < $20,000	17.31	**<.0001**	194.48	**<.0001**	33.54	**<.0001**
Age < 40	17.52	**<.0001**	0.72	0.3946	9.52	**0.0020**
Polysubstance use	--	--	32.41	**<.0001**	66.57	**<.0001**
CES-D ≥ 16	34.19	**<.0001**	--	--	24.44	**<.0001**
Condomless anal sex (UAI)	69.76	**<.0001**	25.14	**<.0001**	--	--