


Substance Use Disorders, Violence, Mental Health, and HIV: Differentiating a Syndemic Factor by Gender and Sexuality

Kiyomi Tsuyuki¹  · Eileen V. Pitpitan¹ · Maria A. Levi-Minzi² · Lianne A. Urada³ · Steven P. Kurtz² · Jamila K. Stockman¹ · Hilary L. Surratt^{2,4}

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Abstract This paper measures syndemic substance use disorder, violence, and mental health and compares the syndemic among HIV-infected heterosexual men, heterosexual women, and men who have sex with men (MSM). Data were from a sample of high needs substance-using, HIV-infected people in South Florida between 2010 and 2012 ($n = 481$). We used confirmatory factor analysis to measure a syndemic latent variable and applied measurement invariance models to identify group differences in the data structure of syndemic co-morbidities among heterosexual men, heterosexual women, and MSM. We found that variables used to measure the syndemic fit each subgroup, supporting that substance use disorder, violence, and mental health coincide in HIV-infected individuals. Heterosexual men and MSM demonstrated similar syndemic latent variable factor loadings, but significantly different item intercepts, indicating that heterosexual men had larger mean values on substance use disorder, anxiety, and depression than MSM. Heterosexual men and heterosexual women demonstrated significantly different syndemic variable factor loadings, indicating that anxiety and

depression contribute more (and substance use contributes less) to the syndemic in heterosexual men compared to heterosexual women. MSM and heterosexual women demonstrated similar syndemic latent variable factor loadings and intercepts, but had significantly different factor residual variances indicating more variance in violent victimization and depression for MSM and more variance in stress for heterosexual women than what is captured by the observed syndemic indicators. Furthermore, heterosexual women had a larger syndemic factor mean than MSM, indicating that the syndemic burden is greater among heterosexual women than MSM. Our findings support that measurement invariance can elucidate differences in the syndemic to tailor interventions to subgroup needs.

Keywords Syndemic · People living with HIV · Measurement invariance model

Introduction

Antiretroviral therapy (ART) has lengthened the lifespan and reduced HIV transmission among people living with HIV (PLWH) [1–6]. However, individuals with socio-structural barriers—such as living in poverty, unstable housing, and with comorbidities like substance use and psychiatric disorders [7–12]—have difficulty adequately engaging in HIV care and achieving viral suppression [1, 13]. Individual-level efforts to engage and retain PLWH in HIV care have limited impact on outcomes as they overlook critical fundamental causes (e.g., socio-structural barriers, life course experiences) [14, 15].

Syndemic theory links adverse socio-structural conditions to co-occurring and synergistic health epidemics that

✉ Kiyomi Tsuyuki
ktsuyuki@ucsd.edu

¹ Department of Medicine, University of California San Diego (UCSD), 9500 Gilman Drive, MC 0507, La Jolla, CA 92093-0507, USA

² Center for Applied Research on Substance Use and Health Disparities, Nova Southeastern University, Miami, FL, USA

³ School of Social Work, San Diego State University (SDSU), San Diego, USA

⁴ Center for Health Services Research, University of Kentucky, Lexington, KY, USA

systemically and disproportionately burden disadvantaged populations [16]. Syndemic theory highlights the socio-structural determinants of health disparities by shifting focus away from individuals and elucidating critical targets for socio-structural intervention. Most applications of syndemic theory to HIV research focus on factors associated with HIV risk [17–25]. However, a growing literature points to syndemic co-morbidities (e.g., depression, drug and alcohol use disorders, violence) as important predictors of HIV transmission risk and HIV treatment outcomes among PLWH [12, 26–31]. Recent research suggests HIV risk reduction interventions are most effective for individuals with syndemic risk [32].

Despite recent advances in syndemic research, two key methodological issues remain with syndemic theory applications. First is the uniform application of syndemic theory to qualitatively different populations, including HIV-negative men who have sex with men (MSM) [17–20], Hispanic women [21], adolescents [22], transgender women [23], patients receiving clinic-based sexually transmitted infection (STI) care [24], female sex workers [25], and members of these subgroups who are living with HIV [12, 26–31]. Although syndemic mental health, substance use disorders, violence, and STIs (including HIV) are related and affect the aforementioned populations as a whole, socio-structural theories point to potential differences by both gender and sexuality. For example, the theory of gender and power suggests that heterosexual women experience gendered power inequities compared to heterosexual men [33, 34]. The minority stress theory suggests that men MSM may experience chronic psychological distress from the fear of stigma based on their sexual identity [35]. Furthermore, enhanced socio-structural inequities and resultant chronic stress can affect heterosexual women and MSM differently.

Research suggests that differences in syndemic co-morbidities exist among heterosexual women, MSM, and heterosexual men. Heterosexual women experience significantly higher rates of depression [36, 37], anxiety [38], and intimate partner violence [39], and lower rates of substance use disorders [40, 41], than heterosexual men. MSM experience higher rates of depression [29, 42], substance use disorders [29, 43], and sexual risk behavior [44] than heterosexual men. Likewise, racial and ethnic minority heterosexual men and MSM may encounter gendered experiences of discrimination and violence (e.g., police, gangs, fights) and can struggle with conforming to masculine ideologies depending on their social context [45–47]. However, no study to date has empirically tested for differences in the syndemic among these groups of PLWH to tailor risk reduction or health interventions to sub-group needs.

A second methodological issue is the lack of researcher consistency in measuring syndemics. Whereas some measure syndemics as a summative count of co-morbidity prevalence [26, 48], others fit syndemic co-morbidities to one latent variable [49, 50]. Summative approaches are simple and generate easy to interpret outcomes [51], but they have several shortcomings that are addressed by the latent variable approach. Summative approaches: (1) do not account for (potential) synergistic effects of the syndemic, ignoring the covariance structure of syndemic data and throwing away information, (2) assume that each co-morbidity contributes equally to the syndemic, and (3) assume that syndemic co-morbidities are the same and combine equally in all population sub-groups [52]. Latent variable approaches capture the full structure of syndemic data, and generate a variable that can be interpreted in light of the syndemic theory [15]. Furthermore, research applying the latent variable approach has found that the same co-morbidities comprise the syndemic for both MSM and heterosexual men, but that each co-morbidity had significantly different weight (e.g., greater factor loadings, stronger association) on the syndemic between groups (e.g., risky sex was lower and violent victimization was greater for MSM vs. heterosexual men) [50].

This paper empirically explores the similarities and differences in syndemic substance use disorder, violent victimization, and mental health among a sample of substance-using heterosexual men, heterosexual women, and MSM living with HIV in South Florida. Although MSM contact is responsible for the bulk of HIV infections among PLWH in South Florida (68% in Broward County and 69% in Miami Dade County), heterosexual contact comprises a sizeable transmission risk category for men (21 and 19%, respectively) and women (85 and 86%, respectively) [53]. This study is among the first to compare the syndemic among three sub-groups of PLWH using structural equation modeling (SEM) confirmatory factor analysis (CFA). Figure 1 shows how we operationalize the syndemic construct. We hypothesize that substance use disorder, violent victimization, and poor mental health will adequately measure the syndemic in all groups. In addition, we hypothesize that each co-morbidity among heterosexual women and MSM (compared to heterosexual men) will have greater item loadings (i.e., stronger association) on the underlying syndemic latent variable.

Methods

Data

Data were collected from a sample of vulnerable, substance-using PLWH in South Florida between 2010 and

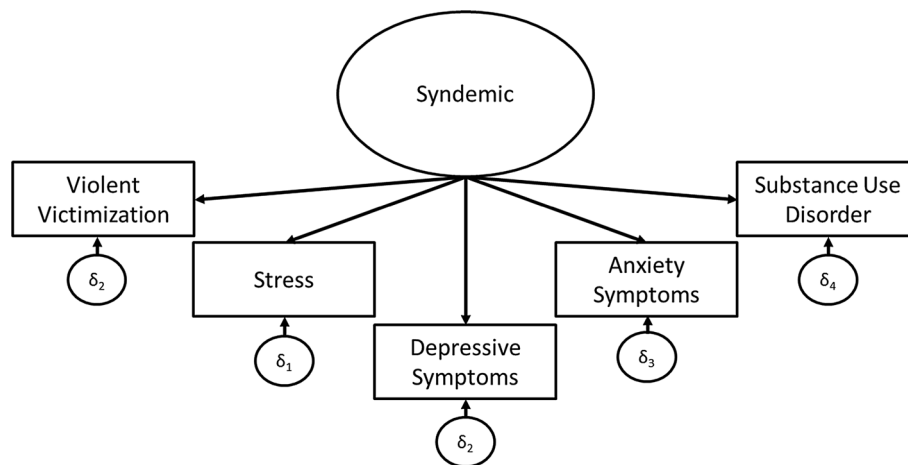


Fig. 1 Multigroup structural equation model of syndemic health comorbidities, South Florida, 2013. Structural model: configural invariance: (1) heterosexual men—AIC = 3175.75, BIC = 3219.11, log-likelihood = -1572.88, (2) MSM—AIC = 3674.49, BIC = 3720.43,

log-likelihood = -1822.25, (3) heterosexual women—AIC = 4490.03, BIC = 4538.73, log-likelihood = -2230.01. AIC Akaike information criterion, BIC Bayesian information criterion

2012 ($n = 503$)—details described elsewhere [10, 54]. Recruitment was guided by targeted sampling—a method used to recruit hard-to-reach populations—in geographic areas with high HIV prevalence and poverty indices [55]. Field staff used direct outreach to recruit indigent HIV-positive substance users through systematic distribution of study cards and flyers in street venues and HIV service organizations within the target areas. Eligibility requirements were: ≥ 18 years old, recent substance use, confirmed HIV-positive, and prescribed ART. Institutional Review Boards of University of Delaware (predecessor institution) and Nova Southeastern University approved study protocols. An NIH Certificate of Confidentiality was obtained. Trained project staff obtained informed consent and then administered face-to-face structured interviews based on the global appraisal of individual needs (GAINs) instrument [56], which assessed demographics, substance use and dependence (DSM-IV-R), and mental health status. Standardized instruments assessed violent victimization and stress, among other HIV-related factors (e.g., diagnosis and treatment history, attitudes toward providers, stigma, and ARV knowledge and adherence). Participants received a \$30 stipend upon interview completion (averaging 1 hour long).

Sample

The analytic sample ($n = 481$) included men and women with information on biological sex, HIV sexual risk behavior, sexual preference (i.e., prefers to have sex with only females, only males, or females and males), and past 90 day sexual activity. We prioritized grouping by sexual risk behavior, beginning with sexual activity and gender of partner in the past 90 days (114 men only had sex with

women, 147 MSM, 168 women had sex with men). Among those with missing data ($n = 58$), we grouped individuals according to sexual preference (18 men preferred sex with women, 10 men preferred sex with men, and 8 women preferred sex with men). One man preferred sex with both men and women (MSMW), but was coded as MSM due to a lack of power to conduct sub-analyses with MSMW. Among those still missing a sexual risk group, we grouped individuals according to transmission of HIV via sexual contact (1 man contracted HIV via heterosexual contact, 14 women contracted HIV via heterosexual contact, and 6 remained missing). Our final analytic sub-groups included 133 heterosexual men, 158 MSM, and 190 heterosexual women.

Measures

The GAINs instrument [57] was used to assess substance use disorder, violent victimization, and mental health variables used to develop the syndemic factor. A *general victimization scale* ($\alpha = 0.86$) measured *violent victimization severity* (analyzed as a continuous variable). Questions included physical, sexual, and emotional violence, the recency of such events, and current worry about violent victimization (15-item scale—0: no victimization to 15: recent, severe victimization) [57].

Mental health was treated as continuous variables in our analysis and measured by scales assessing depression (past year), anxiety (past year), and stress (past 90 days). Depressive symptoms (e.g., feeling sad, lonely, or hopeless; feeling tired or having no energy) were assessed with a nine-item summative scale (0: no/minimal to 9: severe depression; $\alpha = 0.87$) [57]. Anxiety symptoms (e.g., feeling nervous, anxious, or tense; unable to control worries)

were assessed with a 12-item summative scale (0: no anxiety to 12: severe anxiety; $\alpha = 0.87$) [57]. Stress (e.g., go without food, clothing, housing because no money; get divorced or break up with partner) was measured with an adapted crisis in family systems (CRISYS) scale (0: no stress to 8: severe stress; $\alpha = 0.57$) [58]. The poor internal consistency of the stress instrument does not pose a serious issue as our analytic approach (e.g., measurement invariance framework) tests a kind of internal consistency within the latent construct rather than within individual instruments [59].

Substance use disorder (past 12 months) from DSM-IV criteria (11 items measuring drug problem severity, e.g., using more or longer than intended, withdrawal problems; $\alpha = 0.86$) was treated as a continuous variable in our analysis [57].

Data Analysis

Heterosexual men, heterosexual women, and MSM were compared on sociodemographic characteristics and syndemic indicator variables. χ^2 statistic was used for categorical variables and the F-statistic from ANOVA was used for variables treated as continuous to detect statistically significant differences between groups. We then created a scatter plot matrix with correlation coefficients to provide a graphic indication of the covariation between the five comorbidities across groups (Fig. 2). Furthermore, we checked for multivariate outliers as the observed covariance structure and estimated CFA model parameters can be heavily influenced by outliers. Multivariate outliers were accessed using the 15th percentile of the χ^2 distribution as the defined threshold for outliers using MATA with the *bacon*-command in STATA [60, 61]. We did not detect any influential outliers in our sample. We then tested hypotheses with CFA using maximum likelihood estimation and the *sem*-command in STATA 13 [62].

We began by examining the factor structure of the syndemic indicator variables in each group using linear CFA to test for configural invariance. Configural invariance is supported if the model fits the data well in all groups and the pattern of salient and significantly non-zero factor loadings is similar across groups [59]. Establishing configural invariance (in this case that the measured variables are all indicators of a latent, or underlying, syndemic variable) allows for comparison between multiple groups in SEM, by demonstrating that the syndemic indicator variables make up a syndemic latent variable with suitable model fit across groups. To test for configural invariance, we fit the syndemic latent variable with free parameters to each group. For identification purposes, the factor loadings for violent victimization severity were fixed to 1 and the intercept was fixed to 0 to allow for estimating

(identifying) the factor mean [59]. It is noteworthy that the syndemic latent variable has an arbitrary (unitless) non-negative scale. Model fit was assessed by evaluating one incremental fit index [comparative fit index (CFI)] and two absolute fit indices [root mean squared error approximation (RMSEA) and the standardized root mean squared residual (SRMR)]. We chose cut off values of $CFI \geq 0.95$, $RMSEA < 0.06$, and $SRMR \leq 0.08$, as suggested by Hu and Bentler [63].

Once configural invariance was ascertained, we used multiple group CFA to estimate an unconstrained model (Model 1), and to examine metric invariance (Model 2), strong invariance (Model 3), strict measurement invariance (Model 4), and equal factor means (Model 5) in the syndemic latent variable. By estimating a series of nested models that were increasingly restrictive in their assumptions, we compared: (1) MSM to heterosexual men (Table 3), (2) heterosexual women to heterosexual men (Table 4), and (3) MSM to heterosexual women (Table 5). The fit between models was compared using a χ^2 difference test. A non-significant result would indicate that the fit of the constrained model does not differ significantly from the unconstrained model. Once again, for identification purposes, the factor loadings for violent victimization severity were fixed to 1 and the intercept was fixed to 0 to allow for estimating (identifying) the syndemic factor mean [59].

In Model 1, we estimated an *unconstrained model* where factor loadings, item intercepts, and error variances were allowed to vary across groups. In this step, we fitted a single factor model to the covariance matrix of syndemic indicators across groups. In Model 2, we constrained factor loadings for syndemic items to be equal across groups to test for *metric invariance*. A non-significant χ^2 difference test between Models 2 and 1 indicates that metric invariance has been satisfied. Metric invariance introduces the concept of equal metrics across groups and, if achieved, differences in item scores can be meaningfully compared across groups [59]. In Model 3, we further constrained item intercepts to be equal to test for *strong (or scalar) invariance*, which assumes invariance of factor loadings and item intercepts. Strong invariance implies that any group differences in the mean of the observed items are due to differences in the mean of the underlying syndemic construct [59]. A non-significant χ^2 difference test between Models 3 and 2 indicates that the intercepts are invariant across groups. In Model 4, we further constrained error variances (residual variances) to be equal to test for *strict invariance*, which assumes invariance of factor loadings, item intercepts, and item variation. As a result, the amount of the variance in the syndemic indicators that was not explained by the common factor was constrained to be equal across groups. A non-significant χ^2 difference test

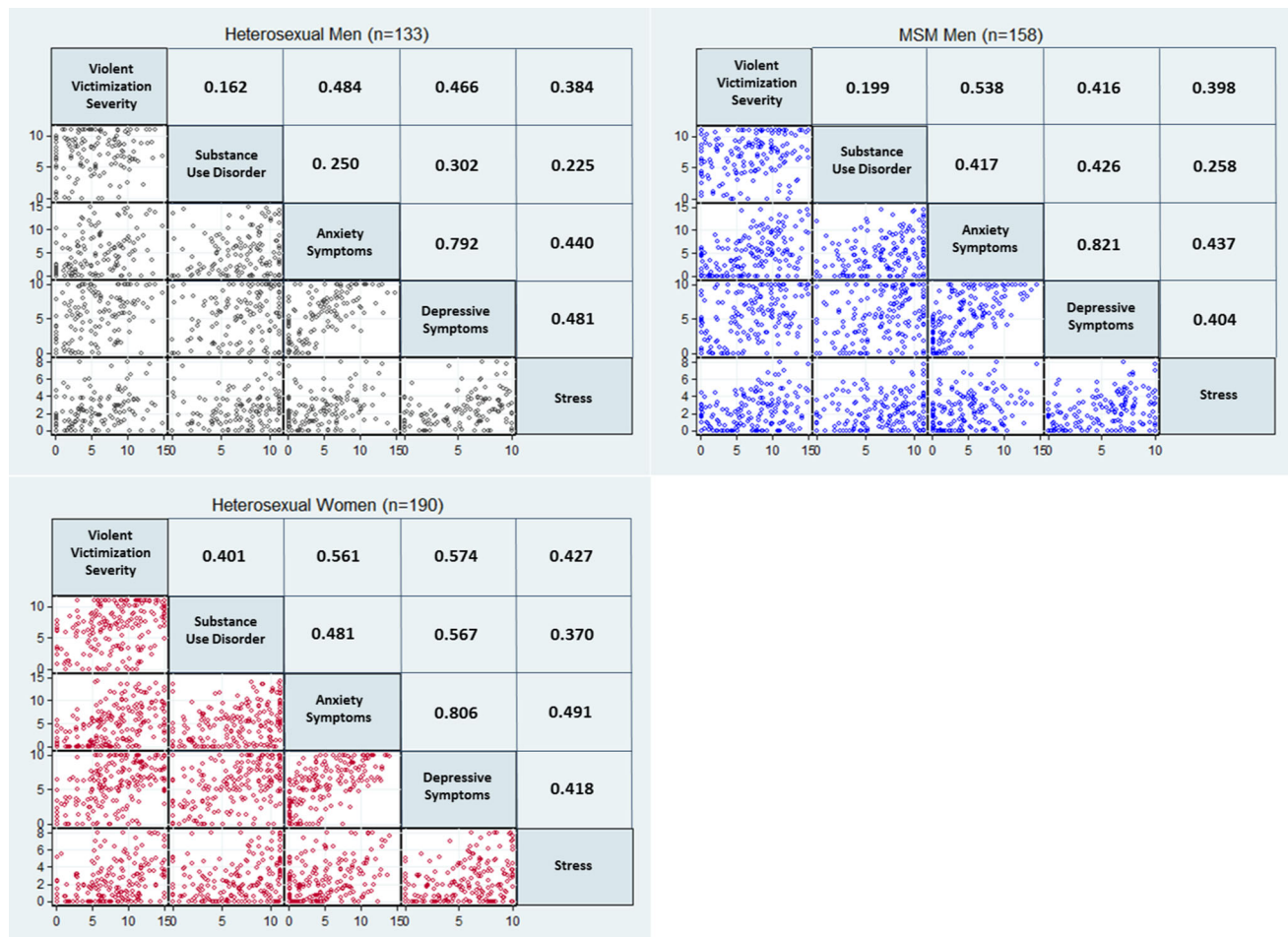


Fig. 2 Scatter plot matrices using jittering with correlation coefficients of syndemic co-morbidities among heterosexual men, MSM, and heterosexual women (n = 481)

between Models 4 and 3 indicates that any observed group differences in the observed syndemic indicators was attributable to a difference with respect to the latent syndemic variable that we measured [64]. In Model 5, we further constrained latent means to be equal across groups.

Results

Sample Characteristics

Table 1 provides a description of the overall study sample (n = 481) by socio-demographic and syndemic variables. In terms of socio-demographic variables, the overall sample averaged 46.13 years old (range = 19–71 years, standard deviation = 7.75) and averaged living with HIV for 12.95 years (range = 0–30 years, standard deviation = 7.31). About half of the sample reported having less than a high school education (44%), the majority were of Black race or African-American (67%), reported a monthly

income of at least \$501 (68%), and almost one-third tested positive for an STI in the past year (29%). In terms of syndemic indicator variables, the sample averaged a moderate level (7.06) on the violent victimization scale (range 0–15, standard deviation = 4.19). The sample had moderate levels of mental health problems with an average of 5.36 depressive symptoms (range 0–9, standard deviation = 3.02), 4.68 anxiety symptoms (range 0–12, standard deviation = 3.66), and 2.18 on the stress scale (range 0–8, standard deviation = 1.85). The sample averaged a high level (6.87) of past year symptoms of substance use disorder (range 0–11, standard deviation = 3.23).

Table 1 also reports significant differences in socio-demographic and syndemic variables by analytic sub-groups (i.e., heterosexual men, MSM, and heterosexual women) with heterosexual men as the comparison group for mean comparisons. On average, MSM were significantly younger (mean age = 44.85) than heterosexual men (mean age = 47.50, $F = 8.55$, $p = 0.004$) and lived significantly more years with HIV (mean years = 14.32) compared to

Table 1 Characteristics and syndemic indicators in adults living with HIV in South Florida

Continuous variables	Total (n = 481)		Heterosexual men (n = 133)		MSM (n = 158)		Heterosexual women (n = 190)	
	M	SD	M	SD	M	SD	M	SD
Age	46.13	7.75	47.50	7.51	44.85**	8.11	46.24	7.47
Years HIV-positive	12.95	7.31	12.49	7.43	14.32*	7.63	12.12	6.82
Violent victimization severity	7.06	4.19	5.53	4.00	7.05**	4.05	8.15***	4.12
Anxiety symptoms (last year)	4.68	3.66	4.51	3.81	4.60	3.50	4.87	3.69
Depressive symptoms (last year)	5.36	3.02	5.15	3.19	5.26	3.06	5.58	2.87
Substance use disorder (last year)	6.87	3.23	7.16	3.10	6.92	3.05	6.64	3.46
Stress (90 days)	2.18	1.85	2.11	1.76	2.13	1.67	2.27	2.04
Categorical variables	n	%	n	%	n	%	n	%
Education***								
High school or more	269	56	59	44	118	75	92	48
Less than high school	212	44	74	56	40	25	98	52
Race/ethnicity***								
Black/African-American	324	67	98	74	79	50	147	77
Non-Hispanic White	68	14	5	4	39	25	24	13
Hispanic/Latino	89	19	30	23	40	25	19	10
Income (\$/month)								
\$501 or more	326	68	84	63	105	66	137	72
\$0–500	155	32	49	37	53	34	53	28
Positive STI (last year)*	139	29	29	22	44	28	66	35
Total	481	100.0	133	29.9	158	30.1	190	40.0

M = mean, SD = standard deviation, F = F-statistic

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ difference between heterosexual men, MSM, and women using χ^2 for comparisons among categorical variables and F-statistic for comparison of mean between MSM, women, and heterosexual men (comparison group)

heterosexual men (mean age = 47.50, $F = 8.55$, $p = 0.004$; mean years with HIV = 12.49, $F = 4.61$, $p = 0.032$). A significantly greater proportion of MSM reported having a high school or more education (75%) than heterosexual men (44%) and heterosexual women (48%, $\chi^2 = 43.11$, $p < 0.001$). Furthermore, a significantly greater proportion of MSM reported being non-Hispanic White (25%), than heterosexual men (4%) and heterosexual women (13%, $\chi^2 = 46.12$, $p < 0.001$). For syndemic variables, MSM (mean score = 7.05, $F = 10.07$, $p = 0.002$) and heterosexual women (mean score = 8.15) reported significantly more violent victimization on average than heterosexual men (mean score = 5.53, $F = 32.39$, $p < 0.001$).

Figure 2 shows the scatter plot matrices and the correlation coefficients for syndemic variables by analytic subgroup (i.e., heterosexual men, MSM, and heterosexual

women). The correlations between syndemic variables are broadly similar in MSM compared to heterosexual men, whereas the correlations between syndemic variables are greater in heterosexual women compared to heterosexual men.

Configural Invariance

Configural invariance for the syndemic we modeled was examined by testing a one-factor solution in each of the three sub-groups (Table 2). In this case, configural invariance examines whether the same items form a syndemic factor in each group. The one factor solution fit well for heterosexual men (CFI = 1.00, RMSEA = 0.00, SRMR = 0.03), MSM (CFI = 0.98, RMSEA = 0.10, SRMR = 0.04), and heterosexual women (CFI = 0.97, RMSEA = 0.11, SRMR = 0.04). Furthermore, the pattern

Table 2 Measurement model of a syndemic factor using confirmatory factor analyses

	Model 1: Heterosexual men (n = 133)		Model 2: MSM (n = 158)		Model 3: Heterosexual women (n = 190)	
	<i>b</i>	SE	<i>b</i>	SE	<i>b</i>	SE
Indicators						
Violent victimization severity ^a	1.00		1.00		1.00	
Substance use disorder (last year)	0.46	0.14	0.61	0.13	0.78	0.11
Anxiety symptoms (last year)	1.53	0.24	1.50	0.20	1.23	0.13
Depressive symptoms (last year)	1.33	0.21	1.17	0.16	0.98	0.10
Stress (90 days)	0.43	0.09	0.35	0.07	0.40	0.06
Syndemic mean	5.53	0.35	7.05	0.32	8.15	0.30
Fit indices						
χ^2 (df)	4.95 (5)	p = 0.422	12.31 (5)	p = 0.031	16.26 (5)	p = 0.01
CFI	1.00		0.98		0.97	
RMSEA	0.00		0.10		0.11	
SRMR	0.03		0.04		0.04	

b factor loadings, *SE* standard error, *CFI* comparative fit index, *RMSEA* root mean squared error approximation, *SRMR* standardized root squared residual

^a Marker variable for identification purposes: factor loading fixed to 1 and intercept fixed to 0. Model estimation stopped once model comparisons are significantly different demonstrating worse model fit

of salient and significantly non-zero factor loadings was similar across groups, indicating support for configural invariance among the three groups.

Metric, Strong, and Strict Invariance

Having established configural invariance for the syndemic variable across all three groups, we next tested invariance with two-group CFAs between: (1) heterosexual men and MSM (Table 3), (2) heterosexual men and heterosexual women (Table 4), and (3) MSM and heterosexual women (Table 5).

Heterosexual Men Versus MSM

For men (Table 3), we first examined *metric invariance* (Model 2) in the syndemic in which factor loadings were

constrained to be equal. The χ^2 difference test (comparing the fit of the constrained model—Model 2—to that of the unconstrained model—Model 1—where factor loadings were free to vary), indicated the syndemic factor loadings could be constrained across groups of men without significantly reducing model fit, $\Delta\chi^2(4) = 2.93$, supporting full metric invariance. Second, we examined *strong invariance* (Model 3) in which item intercepts were constrained to be equal. Strong invariance is a necessary condition for the meaningful comparison of the factor means and, if it holds, it means that differences in the means of the indicators are due to differences in the level of the factor. The χ^2 difference test between Models 3 and 2 was significant, $\Delta\chi^2(4) = 13.43$, indicating that syndemic item intercepts are not equal across heterosexual men and MSM and could not be constrained across groups without significantly reducing model fit. Heterosexual men

Table 3 The results of metric invariance tests of syndemic indicators for heterosexual men and MSM (n = 291)

Model specification ^a	χ^2	df	CFI	RMSEA	SRMR
Model 1: free all parameters	17.26	10	0.99	0.07	0.04
Model 2: metric (loadings)	20.19	14	0.99	0.06	0.05
Model 3: strong (loadings + intercepts)	33.62	18	0.97	0.08	0.05
Model comparisons	$\Delta\chi^2$	Δ df	Δ CFI		p-values
Model 2 – Model 1 (metric invariance)	2.93	4	0.00		0.57
Model 3 – Model 2 (strong invariance)	13.43	4	–0.22		0.01

CFI comparative fit index, *RMSEA* root mean squared error approximation, *SRMR* standardized root mean squared residual

^a Marker variable for identification purposes: factor loading fixed to 1 and intercept fixed to 0. Model estimation stopped once model comparisons are significantly different demonstrating worse model fit

Table 4 The results of metric invariance tests of syndemic indicators for heterosexual men and heterosexual women (n = 323)

Model specification ^a	χ^2	df	CFI	RMSEA	SRMR
Model 1: free all parameters	21.22	10	0.98	0.08	0.03
Model 2: metric (loadings)	35.13	14	0.97	0.10	0.07
Model comparisons	$\Delta\chi^2$	Δ df	Δ CFI	p-values	
Model 2 – Model 1 (metric invariance)	13.91	4	–0.02	0.01	

CFI comparative fit index, RMSEA root mean squared error approximation, SRMR standardized root mean squared residual

^a Marker variable for identification purposes: factor loading fixed to 1 and intercept fixed to 0. Model estimation stopped once model comparisons are significantly different demonstrating worse model fit

had significantly larger item intercepts for substance use disorder (intercept = 4.63, 95% CI 3.0, 6.27), anxiety (intercept = –3.97, 95% CI –6.69, –1.26), and depression (intercept = –2.23, 95% CI –4.65, 0.19) than MSM (substance use disorder intercept = 2.61, 95% CI 0.76, 4.45, anxiety intercept = –6.00, 95% CI –8.83, –3.18, depression intercept = –3.02, 95% CI –5.34, –0.71) (data not shown). These results suggest that the same syndemic latent factor is being measured across heterosexual men and MSM, but that the item means (expected item values when the value of the factors is equal to zero) of substance use disorder, anxiety, and depression is greater for heterosexual men than MSM. We cannot compare latent means because we did not achieve intercept invariance.

Heterosexual Men Versus Heterosexual Women

A two-group CFA for the syndemic was then conducted with heterosexual men and heterosexual women (Table 4). We first examined *metric invariance* (Model 2) in the

syndemic (factor loadings were constrained to be equal). The χ^2 difference test—comparing the fit of the constrained model (Model 2) to that of the unconstrained model (Model 1)—indicated that the syndemic factor loadings could not be constrained to be equal across groups without significantly reducing model fit, $\Delta\chi^2(4) = 13.91$. This finding does not support metric invariance between heterosexual men and heterosexual women, indicating that heterosexual men and heterosexual women have different factor loadings on syndemic latent variable indicators. Upon further analysis of the syndemic latent variable, the factor loadings for heterosexual women are larger for substance use disorder (loading = 0.77, 95% CI 0.57, 0.99) and smaller for anxiety (loading = 1.23, 95% CI 0.99, 1.48) and depression (loading = 0.98, 95% CI 0.79, 1.18) than for heterosexual men (substance use disorder loading = 0.46, 95% CI 0.18, 0.73, anxiety loading = 1.53, 95% CI 1.07, 2.00, depression loading = 1.33, 95% CI 0.92, 1.75) (data not shown). These results suggest that the same syndemic latent factor is being measured across heterosexual men and heterosexual women, but that substance use disorder may contribute more, and mental health less to the overall syndemic for heterosexual women than for heterosexual men.

MSM Versus Heterosexual Women

A two-group CFA for the syndemic was then conducted with MSM and heterosexual women (Table 5). We first examined *metric invariance* (Model 2) in the syndemic in which factor loadings were constrained to be equal. The χ^2 difference test—comparing the fit of the constrained model (Model 2) to that of the unconstrained model (Model 1) where factor loadings were free to vary—indicated the syndemic factor loadings could be constrained across groups of men without significantly reducing model fit, $\Delta\chi^2(4) = 8.16$, supporting full metric invariance. Second,

Table 5 The results of metric invariance tests of syndemic indicators for MSM and heterosexual women (n = 348)

Model specification ^a	χ^2	df	CFI	RMSEA	SRMR
Model 1: free all parameters	28.57	10	0.97	0.10	0.04
Model 2: metric (loadings)	36.73	14	0.97	0.10	0.06
Model 3: strong (loadings + intercepts)	45.17	18	0.96	0.09	0.06
Model 4: strict (loadings + intercepts + residuals)	58.25	23	0.95	0.09	0.05
Model comparisons	$\Delta\chi^2$	Δ df	Δ CFI	p-values	
Model 2 – Model 1 (metric invariance)	8.16	4	–0.01	0.09	
Model 3 – Model 2 (strong invariance)	8.44	4	–0.01	0.08	
Model 4 – Model 3 (strict invariance)	13.08	5	–0.01	0.02	

CFI comparative fit index, RMSEA root mean squared error approximation, SRMR standardized root mean squared residual

^a Marker variable for identification purposes: factor loading fixed to 1 and intercept and residual variance fixed to 0. Model estimation stopped once model comparisons are significantly different demonstrating worse model fit

we examined *strong invariance* (Model 3) in which intercepts were constrained to be equal. The χ^2 difference test between Models 3 and 2 indicated syndemic factor loadings and intercepts could be constrained across groups without significantly reducing model fit, $\Delta\chi^2(4) = 8.44$, supporting strong invariance and that differences in the means of the indicators are due to differences in the level of the factor. Third, we examined *strict invariance* in the syndemic in which residual variances were also constrained to be equal (Model 4). The χ^2 difference test between Models 4 and 3 indicated syndemic factor loadings, intercepts, and residual variances could not be constrained across groups without significantly reducing model fit, $\Delta\chi^2(4) = 13.08$, not supporting strict invariance. MSM had larger residual variances for violent victimization (11.52, 95% CI 9.13, 14.53) and depressive symptoms (2.37, 95% CI 1.73, 3.26) than heterosexual women (violent victimization = 10.15, 95% CI 9.13, 14.53, depressive symptoms = 1.43, 95% CI 0.92, 2.23) and heterosexual women had larger residual variances for stress (3.07, 95% CI 2.49, 3.79) than MSM (2.14, 95% CI 1.71, 2.69) (data not shown). Furthermore, heterosexual women had a larger factor mean (7.80, 95% CI 7.29, 8.30) for the syndemic latent variable than MSM (7.53, 95% CI 7.00, 8.06). These results suggest that the syndemic is comprised of similar indicators, but that there is more variance in violent victimization (MSM), depression (in MSM) and stress (heterosexual women) than captured by the observed items. Furthermore, it appears that the syndemic comprises a similar structure between MSM and heterosexual women, but is larger among heterosexual women than among MSM.

Discussion

This study elucidated a syndemic latent variable in a sample of vulnerable PLWH in South Florida with several key findings. First, the variables used to measure the syndemic appropriately fit each sub-group, which supports research that substance use disorder, violence, and mental health all coincide to create a syndemic in people with HIV. Second, we empirically identify differences in the syndemic between our three sub-groups. Heterosexual men and MSM demonstrated similar syndemic latent variable factor loadings, but significantly different item intercepts. Heterosexual men and heterosexual women demonstrated significantly different similar syndemic latent variable factor loadings, with greater loadings for anxiety and depression in heterosexual men and a greater loading for substance use disorder in heterosexual women. MSM and heterosexual women demonstrated similar syndemic latent variable factor loadings and intercepts, but they had

significantly different residual variances and factor means. We situate these findings within the syndemic literature and highlight methodological implications for future syndemic research among PLWH in order to better tailor HIV care and risk reduction interventions to these sub-groups to improve engagement and retention of vulnerable populations in HIV care.

This is one of the first studies to measure the syndemic among PLWH [12, 26–31], whereas most syndemic studies are among individuals at risk for HIV [17–25]. Results support the co-occurrence of substance use disorder, violence, and mental health in a vulnerable sample of substance-using PLWH. In a review of the convergence of HIV, substance use disorders, and mental health among PLWH, Walkup et al. [65] cite numerous studies that support the co-occurrence of these morbidities [65]. For example, in a national probability sample of PLWH in medical care in the US (HIV cost and services utilization study) nearly half (48%) reported recent depressive, anxiety, or panic symptoms and almost 40% used illicit drugs (other than marijuana), with 12% screening as substance dependent [66]. Although over half (61%) utilized mental health or substance abuse treatment (prior 6 months) [67], another study found that patient depression was underdiagnosed among those in HIV care [68]. It is especially critical to diagnose and treat substance use disorders and mental health problems among PLWH given their potentially detrimental effects on HIV care outcomes [65]. Furthermore, violent victimization was a key co-morbidity of the syndemic in our analysis. A trauma-informed model of care for PLWH is necessary [69] in order to diagnose and address the effects that intimate partner violence and child sexual abuse may have on engagement in HIV care and ART adherence [70, 71].

Despite the syndemic consistently being comprised of substance use disorder, violence, and mental health, this study found that heterosexual men, MSM, and heterosexual women may experience the syndemic differently. For example, our analysis revealed that heterosexual men and MSM demonstrated similar syndemic latent variable factor loadings, but significantly different item intercepts. Heterosexual men had significantly larger item intercepts for substance use disorder (4.63), anxiety (−3.97), and depression (−2.23) compared to MSM (substance use disorder = 2.61, anxiety = −6.00, and depression = −3.02). This finding indicates that heterosexual men have a greater item mean, or expected item value when the factor item value is equal to zero, for substance use disorder, anxiety, and depression compared to MSM. Our study extends upon findings that syndemics undermine health and persist across the lifetime of heterosexual men, as well as MSM [72]. It is furthermore critical to approach men's (both heterosexual men and MSM) health

holistically by addressing the socio-structural inequities they face that may drive their health behavior and exacerbate their syndemic risk [73].

We also found that the underlying syndemic factor structure for heterosexual women was similar to that of heterosexual men, confirming the syndemic may comprise substance use disorder, violence, and mental health for both groups. However, we find heterosexual men and heterosexual women demonstrated significantly different syndemic latent variable factor loadings. Upon further analysis of the syndemic latent variable, we found that heterosexual men had greater loadings for anxiety (1.53) and depression (1.33) and smaller loadings for substance use disorder (0.46) than heterosexual women (anxiety = 1.23, depression = 0.98, substance use disorder = 0.77). Our findings indicate that systemic integration of screening and care for substance use disorder and mental health co-morbidities for heterosexual men and heterosexual women living with HIV will maximize yields in positive outcomes [65]. Moreover, the integration of services can serve to supplement, rather than replace, specialty services in that men and women with severe diagnoses can receive continued long-term care through specialty services [65].

We found that the syndemic had the same underlying factor structure for MSM as for heterosexual women, but our analysis revealed that MSM had significantly greater factor residual variances for violent victimization and depressive symptoms and lower factor residual variances for stress than heterosexual women. This finding suggests that there is more variance in violent victimization and depression for MSM and stress for heterosexual women than what is captured by the observed syndemic indicators. Moreover, heterosexual women had a larger syndemic factor mean than MSM, which indicates that the syndemic burden of experiencing multiple comorbidities is larger among heterosexual women than among MSM.

By identifying differences in the syndemic among PLWH, we can tailor healthcare to sub-group needs. This allows us to: (1) enhance diagnosis of depression, anxiety, and stress and improve patient linkage to mental health care and treatment [65], which may also improve adherence and linkage to care [74, 75], and (2) enhance substance use disorder diagnosis and linkage to treatment, thereby reducing risky behavior associated with substance use disorder and improving adherence and linkage to HIV care [65]. Multiple group SEM has been used in other research to examine how socioeconomic status differentially affects mental health by race and ethnicity, age, and gender [76] and how stress and coping measures differ by race in PLWH [77]. To our knowledge, measurement invariance modeling has only been applied to syndemics in one other study to identify syndemic differences between

MSM, men who have sex with men and women (MSMW), and heterosexual men [50].

Limitations and Strengths

Findings must be considered in light of several important limitations. First, this is a cross-sectional study therefore limiting any assertions of causality. Adverse childhood experiences, including childhood sexual abuse and trauma, are correlated with increased disease and adoption of risky behaviors later in life. However, few studies apply the life course perspective to syndemic HIV research to understand how these traumatic experiences link to syndemic risk later in life. Likewise, understanding the developmental trajectory of the syndemic would ascertain the causal effect of syndemic co-morbidities on the underlying syndemic factor and identify life course targets to address unmet need for prevention and care in vulnerable populations. Second, our study sample is a highly specific group of vulnerable PLWH in South Florida, therefore also limiting the generalizability of findings to other groups of people or regions in the US. Third, the study utilized face-to-face in-depth surveys to collect data, which may lend to an interviewer effect or social desirability bias. Nevertheless, research has found that face-to-face interviews are more effective than telephone interviews and equally as effective as computer-based interviews in surveying about drug and alcohol use [78] and psychological distress [79].

Summary Statement

This study measured the syndemic among heterosexual men, heterosexual women, and MSM. We found that substance use disorder, violence, and mental health all coincide to create a syndemic in PLWH. We also identified differences in the syndemic between sub-groups. These findings indicate that substance use disorder, violence, and mental health may co-vary differently among sub-groups to make up distinct syndemics, which require tailored attention by health care providers.

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Compliance with Ethical Standards

Conflict of interest Kiyomi Tsuyuki, Eileen V. Pitpitan, Maria A. Levi-Minzi, Lianne A. Urada, Steven P. Kurtz, Jamila K. Stockman and Hilary L. Surratt 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 Review Boards of the University of Delaware (predecessor institution) and Nova Southeastern University and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. An NIH Certificate of Confidentiality was acquired and informed consent was obtained from every participant prior to interview.

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