HIV Sexual Risk and Syndemics among Women in Three Urban Areas in the United States: Analysis from HVTN 906

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ABSTRACT *Limited data are available on the longitudinal occurrence of syndemic factors among women at risk for HIV infection in the USA and how these factors relate to sexual risk over time. HVTN 906 was a longitudinal study enrolling 799 HIV-uninfected women in three cities. Assessments were done at baseline, 6, 12, and 18 months to assess syndemic factors (low education, low income, unemployment, lack of health insurance, housing instability, substance use, heavy alcohol use, partner violence, incarceration) and sexual risk outcomes. For each sexual risk outcome, a GEE model was fit with syndemic factors or syndemic score (defined as sum of binary syndemics, ranging from 0 to 9), visit, study site, age and race/ethnicity as predictors to examine the multivariable association between syndemic factors and outcomes over time. Odds of unprotected sex while drunk or high were significantly higher when women reported lack of health insurance, substance and heavy alcohol use and partner violence. Housing instability, substance and heavy alcohol use, partner violence and recent incarceration were associated with higher odds of having multiple sexual partners. Odds of sex exchange were significantly higher in the presence of unemployment, housing instability, low education, lack of health insurance, substance and heavy alcohol use, partner violence and incarceration. Housing instability, substance and heavy alcohol use, and partner violence were significantly associated with higher odds of unprotected anal sex. Odds of having a recent STI were significantly higher when women reported housing instability and partner violence. There were significantly higher odds of the reporting of any risk outcomes during follow-up with higher syndemic score. This study highlights a group of women experiencing multiple poor social and health outcomes who need to be the focus of comprehensive interventions.*

KEYWORDS *Women, HIV, Syndemics, Sexual risk*

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INTRODUCTION

In 2011, women accounted for 21 % of all new HIV diagnoses in the USA.¹ The vast majority (86 %) of infections among women were acquired through heterosexual contact.¹ African American and Latina women are disproportionately affected by HIV, with rates of new HIV infections 20 times and 4 times higher, respectively, compared to white women.¹

Sexual risk behavior, alcohol and drug use, and abuse and violence victimization come together as synergistic epidemics^{2,3} to enhance significantly the probability of HIV infection among women.⁴⁻⁶ In addition, social and economic disadvantage, homelessness, and incarceration have been shown to be associated with sexual risk behavior and HIV infection.⁷⁻¹⁶ Partner-related or sexual network factors have also been shown to be important in HIV risk among women, including sexual partner drug use, partner incarceration, concurrent sexual partnerships and assortative mixing (e.g., sex with other people from the same race and/or ethnicity).^{7,9,17-20} Limited data are available on the longitudinal occurrence of syndemic factors among women and how these factors relate to sexual risk over time.²¹ Increasing our knowledge of these relationships can help guide screening approaches for syndemic factors and address these interacting factors in designing HIV prevention interventions.

HVTN 906 was an observational cohort study in three urban areas designed to determine the feasibility of recruiting a cohort of US women at high risk of HIV infection for HIV vaccine efficacy trials.^{22,23} The longitudinal data in HVTN 906 provided the opportunity to assess changes in syndemic factors and sexual risk in a cohort of women at risk for HIV infection followed over 18 months and to assess the relationship between syndemic factors and sexual risk over time.

METHODS

HVTN 906 was conducted in Chicago, New York City and Philadelphia, described in detail previously.^{22,23} The protocol and informed consent documents were approved by the Institutional Review Boards for each participating institution. HIV-uninfected women were eligible if they were between the ages of 18 to 45, not pregnant and not intending to become pregnant for 18 months, met high-risk behavioral criteria, and provided informed consent. High-risk behavior was defined as reporting unprotected vaginal or anal sex with a male partner in the prior six months and (1) residing or engaging in risk behaviors (unprotected sex, exchange of sex, or crack cocaine use) within a city-specific geographic high-risk pocket; and/or (2) having a male partner who had: (a) been incarcerated in the last year; (b) injected drugs in the last year; or (c) had concurrent sex with another partner in the last 6 months.

For recruitment, each site identified neighborhoods with the highest rates of new HIV infections among women. The Chicago site focused on identifying and recruiting from sexual networks that included HIV-positive members through street outreach and use of a modified respondent driven sampling scheme. The New York City site identified specific locations for potential recruitment and flyer placement based on local reports, interviews with community-based organizations and brief street interviews, as well as recruiting at bus stops for visitor transportation to upstate prisons, and in visitor waiting areas of jails and prisons. At the Philadelphia site, local ethnographers identified street locations where drugs were sold or

exchanged for sex. Some women reporting high-risk behaviors at prescreening referred their women friends. At the New York City and Philadelphia sites, men with a history of HIV infection, injection drug use, recent incarceration, concurrent partners or having sex with men were identified and asked to refer their female sexual partners.

Study Visits

At the screening visit, women completed a standardized, close-ended interviewer-administered questionnaire in English on demographics, behavioral risks in the prior 6 months, pregnancy history, and current contraception use. Pregnancy and HIV antibody tests were administered along with risk reduction counseling by a different staff member trained in HIV counseling and testing. Enrollment of eligible HIV-uninfected women, who were not pregnant, took place 7–28 days after the screening visit. Follow-up visits were scheduled every 6 months for 18 months to collect questionnaire data as at baseline and to conduct HIV and pregnancy counseling and testing.

Outcome Measures

Five measures were utilized as outcomes. Participants were asked about their total number of male sexual partners in the prior 6 months which was dichotomized at the median value of three partners. Dichotomous outcome variables were constructed for unprotected anal sex, unprotected vaginal or anal sex while they or their partner were drunk or high, and vaginal or anal sex in exchange for money, drugs, or other goods or services. Finally, a dichotomous outcome variable was created based on the self-reported diagnosis or treatment for any sexually transmitted infection (STI) (defined as chlamydia, gonorrhea, syphilis, genital or rectal herpes, genital or rectal warts, or pelvic inflammatory disease) in the prior 6 months.

Syndemic Factors

Measures of social and economic status included education, income, employment, health insurance and housing. Low education was defined as not completing high school. Low income was defined as an annual income of less than \$10,000. Lack health insurance was defined as no private or government insurance. Housing instability was defined as spending at least one night in the prior 6 months in a shelter, transitional housing, or temporary housing or at no fixed address.

Questions on substance use included the frequency and amount of alcohol use, occurrence of injection drug use, and frequency of marijuana, crack cocaine, powder cocaine, amphetamine, heroin, and hallucinogen use in the prior 6 months. Substance use was defined as using any injected or non-injected drugs. Most (97 %) of the women using substances reported use of one or more drugs at least once a month. Heavy alcohol use was defined as drinking four or more drinks daily or drinking 6 or more drinks on a typical day that the woman consumed alcohol.²⁴ Recent incarceration variable defined as spending at least one night in jail or prison in the last 6 months.

We assessed experience of partner violence with four questions drawn from a variety of scales²⁵ that tapped experiences of (1) forced or coerced vaginal and/or anal sex by any male partner, (2) physical assault (“hit, slap, shove, choke, kick, or shake”) or injury/pain (physically hurt”) by a main partner, (3) denigration (“put you down, call you names repeatedly”) and/or control (“control your behavior”) by

a main partner, and (4) fear (“frightened for your safety, or that of your family or friends, because of this man’s anger or threats”) by a main partner.

Statistical Analysis

The prevalence of each syndemic factor and sexual risk outcome (three or more sexual partners, unprotected anal sex, unprotected vaginal or anal sex while they or their partner were drunk or high, vaginal or anal exchange sex, and STI) was summarized at each visit. In addition, we categorized each syndemic factor at one of three groups reflecting the level of influence: individual (substance use, heavy alcohol use), dyadic (partner violence) or structural (unemployment, low income, housing instability, low education, lack of health insurance, and history of incarceration). We then examined whether each woman experienced none, one, two or all three of the syndemic groups. We also created a syndemic score defined as the sum of the binary syndemics, ranging from 0 to 9.

Bivariate relationships among the syndemic factors at baseline were assessed by calculating odds ratios and 95 % confidence intervals. Change in syndemic factors and outcomes over time was characterized using generalized estimating equation (GEE) models with effects for visit, site, age and race/ethnicity (Latina, Non-Latina Black, Non-Latina Non-Black).

To examine the association between each risk outcome and syndemics over time, we fit GEE models with time-varying syndemic predictors and effects for visit, site, age, and race/ethnicity. We considered three parameterizations of syndemic factors: indicators for each syndemic factor, continuous syndemic score (from 0 to 9), and syndemic factor groups (0 or 1, 2, 3), and compared model fit using quasiliikelihood under the independence model criterion (QIC).²⁶ We present models with time-varying syndemic predictors corresponding to the same time period as the risk behavior outcome (e.g., risk reported at 6 months, syndemics reported at 6 months); additionally, we examined models with fixed baseline syndemic predictors.

All GEE models used a logit link function and independent correlation structure. Missing data were not imputed. Statistical significance was defined as $p < 0.05$, with no adjustment for multiple testing. SAS 9.2 was used for data analysis.

RESULTS

Baseline Outcomes and Syndemic Factors

A total of 799 women were enrolled between January 2009 and May 2010. The median age was 37 years; 79.1 % were African American and 15.3 % Latina. About half (54.7 %) of women had three or more male partners; 74.1 % had unprotected sex while they or their partner were drunk or high; 52.2 % exchanged sex for money, drugs, goods, or other services; 24.3 % had unprotected anal sex; and 10.4 % reported having a recent STI (Table 1).

A large proportion (84.7 %) of the women were unemployed, 80.6 % had an annual income of less than \$10,000, 54.4 % had unstable housing in the prior 6 months, 49.3 % had less than a high school degree, and 33.9 % lacked health insurance (Table 1). In the 6 months prior to enrollment, 74.5 % of the women used injected or non-injected substances, 31.0 % were heavy alcohol users, 31.0 % had experienced partner violence and 17.3 % had been in jail or prison. The mean number of syndemic factors was 4.6 (SD=1.91). When examining groups of

TABLE 1 Sexual risk and syndemic factors in prior 6 months by study visit, HVTN 906 (*n*=799)

	Baseline		6 months	12 months	18 months
	<i>n</i> =799		<i>n</i> =686	<i>n</i> =661	<i>n</i> =662
	<i>N</i>	%	%	%	%
Sexual risk behaviors in last 6 months					
Unprotected sex while drunk/high	592	74.1	53.4*	49.0*	45.1*
>3 male partners (median value)	437	54.7	31.2*	28.6*	29.0*
Exchange of sex	417	52.2	37.0*	35.6*	33.1*
Unprotected anal sex	194	24.3	12.4*	11.3*	8.9*
Sexually transmitted infection	83	10.4	5.4*	4.5*	5.5*
Syndemic factors in last 6 months					
Unemployment	677	84.7	82.4	82.2	79.1*
Low income (< \$10,000) ^a	632	80.6	—	—	—
Housing instability	435	54.4	43.4*	41.8*	37.2*
Low education (not HS graduate) ^a	394	49.3	—	—	—
Lack of health insurance ^a	270	33.9	—	—	—
Substance use	595	74.5	60.8*	57.9*	56.6*
Heavy alcohol use	248	31.0	20.7*	20.6*	19.5*
Partner violence	248	31.0	17.8*	16.0*	14.4*
Incarceration	138	17.3	11.5*	8.0*	7.6*
Number of syndemic factor groups ^b					
0	16	2.0	2.6	2.6	3.5
1	126	15.9	32.0	32.5	35.0
2	453	56.7	51.5*	53.3*	50.5*
3	204	25.5	14.0*	11.6*	11.1*

One GEE model was fit for each sexual risk behavior and syndemic factor with measurements at multiple visits.

**p*<0.01 for difference from baseline using a GEE model controlling for site, age and race/ethnicity; for number of syndemic factor groups, 0–1 and 2–3 factors were combined

^aMeasured only at baseline

^bSyndemic factor groups were individual (substance use, heavy alcohol use), dyadic (partner violence), and structural (unemployment, low income, housing instability, low education, no health insurance, incarceration)

syndemic factors (individual, dyadic or structural), 17.9 % of women reported none or one syndemic factor groups, 56.7 % reported two syndemic factor groups and 25.5 % reported all three syndemic factor groups. Among women reporting one syndemic group, 94 % reported structural-level factors. Among women reporting two syndemic groups, 91 % reported structural and individual-level factors.

At baseline, many of the syndemic factors were significantly associated with each other (Table 2). Substance use was significantly associated with all other syndemic factors. In addition, heavy alcohol use was significantly associated with unemployment and lack of health insurance. Measures of social and economic status were almost all significantly associated with each other. Incarceration was significantly associated with unemployment, low income, housing instability and lack of health insurance. Partner violence was significantly associated with housing instability.

Longitudinal Analyses of Sexual Risk Behavior Outcomes and Syndemic Factors

Retention was 79.5 % at 18 months. Sexual risk outcomes and syndemic factors at baseline among those completing and not completing the 18-month visit were

TABLE 2 Association between each syndemic variable at baseline, HVTN 906

Variable (in last 6 months)	Unemployed	Low income	Housing instability	Low education	Lack of health insurance	Substance use	Heavy alcohol use	Partner violence
	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)
Low income	7.73 (5.04, 11.86)	–						
Housing instability	5.34 (3.39, 8.41)	2.84 (1.96, 4.12)	–					
Low education	2.68 (1.77, 4.07)	2.58 (1.77, 3.77)	1.82 (1.37, 2.42)	–				
Lack of health insurance	0.93 (0.632, 1.39)	2.42 (1.57, 3.72)	2.00 (1.48, 2.71)	1.45 (1.08, 1.95)	–			
Substance use	2.91 (1.95, 4.34)	2.58 (1.78, 3.75)	2.71 (1.95, 3.77)	1.93 (1.40, 2.68)	5.62 (3.53, 8.93)	–		
Heavy alcohol use	1.62 (1.03, 2.54)	1.34 (0.90, 2.00)	1.30 (0.96, 1.76)	1.23 (0.91, 1.66)	1.98 (1.45, 2.70)	3.51 (2.29, 5.39)	–	
Partner violence	1.38 (0.89, 2.15)	0.83 (0.57, 1.21)	1.87 (1.37, 2.55)	0.90 (0.67, 1.22)	1.15 (0.84, 1.57)	1.54 (1.07, 2.21)	1.38 (1.00, 1.90)	–
Incarceration	3.94 (1.80, 8.65)	1.86 (1.08, 3.20)	$p<0.0001^a$	1.37 (0.95, 1.98)	3.53 (2.42, 5.16)	6.00 (2.99, 12.03)	1.33 (0.90, 1.95)	1.18 (0.80, 1.74)

^aOR undefined due to zero cell; 0 women were in incarceration who had stable housing

similar except with respect to housing instability (82.4 % 18-month retention among those with stable housing vs. 76.3 % among those with unstable housing; Chi-square $p=0.035$).

Sexual risk behaviors declined over time with the percent of women reporting sexual risk at follow-up visits significantly lower than at baseline (Table 1). The greatest change occurred between baseline and the 6-month visit. In addition, the percent of women reporting syndemic factors was significantly lower than at baseline, with the greatest change occurring between baseline and the 6-month visit, except for unemployment which was consistent over the first 12 months of follow-up.

Estimates from models with time-varying versus baseline syndemic predictors were similar, with somewhat more extreme associations detected using time-varying predictors (baseline predictor models not shown). As assessed by QIC, the syndemic parameterization fit varied for each risk outcome, with syndemic indicators or number of factor groups generally fitting best (data not shown). Higher syndemic score, adjusted for demographics and visit, was significantly associated with higher odds of reporting each of the sexual risk outcomes (Table 3). A higher number of syndemic factor groups, adjusted for demographics and visit, was associated with higher odds of reporting each of the sexual risk outcomes (Table 3). Multivariate models including an indicator for each syndemic factor, with adjustment for demographics and visit, provide a more detailed assessment of the associations. Odds of unprotected sex while drunk or high were significantly higher when women reported lack of health insurance, substance and heavy alcohol use and partner violence. Housing instability, substance and heavy alcohol use, partner violence and recent incarceration were associated with higher odds of having multiple sexual partners. Odds of sex exchange were significantly higher in the presence of unemployment, housing instability, low education, lack of health insurance, substance and heavy alcohol use, partner violence and incarceration. Housing instability, substance and heavy alcohol use, and partner violence were significantly associated with higher odds of unprotected anal sex. Odds of having a recent STI were significantly higher when women reported housing instability and partner violence.tgroup1

DISCUSSION

Findings from this cohort of predominately African American and Latina women at risk of HIV infection indicate that a high proportion of the women experienced syndemic factors. Furthermore, these syndemic factors were associated with a range of sexual risk outcomes. While other studies have found these associations, this longitudinal study provides evidence of persistent effects of the syndemic factors over time. To our knowledge, this is the first analysis that has evaluated relations among syndemic factors at multiple levels, individual, dyadic and structural, over time among high-risk, urban-dwelling women of color.

A high proportion of women experienced significant structural barriers, including unemployment, poverty, housing instability, and low education. Recent incarceration was experienced by one in six women, as observed in other samples of urban women.^{16,27} Many of these structural factors are correlated with each other. Further, these structural barriers were associated with substance use and incarceration, illustrating the overlapping nature of challenges facing the women. Addressing the structural factors that are associated with increased odds of engaging

TABLE 3 Longitudinal analysis of the association of syndemic factors with sexual risk behavior outcomes over time

Sexual risk behavior outcomes (in last 6 months)					
Syndemic factor (in last 6 months)	Unprotected sex while drunk/high		>3 sexual partners		Sexually transmitted infection
	AOR ^a (95 % CI)		AOR ^a (95 % CI)	Exchange of sex AOR ^a (95 % CI)	Unprotected anal sex AOR ^a (95 % CI)
Syndemic score	1.75 (1.61, 1.91)		1.56 (1.43, 1.69)	1.91 (1.74, 2.10)	1.23 (1.11, 1.36)
Number of syndemic groups					
0-1	REF		REF	REF	REF
2	9.59 (7.31, 12.58)		5.16 (3.84, 6.94)	7.82 (5.56, 10.98)	1.66 (1.07, 2.59)
3	35.43 (23.34, 53.78)		9.01 (6.25, 12.99)	17.33 (11.45, 26.23)	2.48 (1.50, 4.11)
Unemployment	0.91 (0.66, 1.26)		1.36 (0.99, 1.89)	1.68 (1.20, 2.35)	0.91 (0.56, 1.48)
Low income	0.84 (0.61, 1.16)		1.16 (0.81, 1.66)	0.98 (0.66, 1.45)	1.17 (0.71, 1.93)
Housing instability	1.00 (0.79, 1.26)		1.47 (1.16, 1.86)	1.82 (1.40, 2.35)	1.64 (1.14, 2.37)
Low education	1.23 (0.96, 1.58)		0.95 (0.74, 1.23)	1.41 (1.07, 1.87)	0.97 (0.69, 1.37)
Lack of health insurance	1.61 (1.16, 2.22)		1.27 (0.92, 1.76)	1.55 (1.12, 2.15)	0.79 (0.49, 1.27)
Substance use	10.48 (8.05, 13.66)		3.61 (2.74, 4.76)	5.95 (4.37, 8.08)	1.26 (0.82, 1.95)
Heavy alcohol use	3.13 (2.34, 4.20)		1.63 (1.24, 2.12)	1.72 (1.29, 2.31)	1.24 (0.83, 1.83)
Partner violence	2.65 (1.96, 3.57)		1.83 (1.41, 2.38)	2.27 (1.69, 3.06)	1.58 (1.12, 2.24)
Incarceration	1.18 (0.79, 1.77)		1.63 (1.15, 2.30)	1.50 (1.02, 2.22)	1.40 (0.89, 2.20)

^aControlling for visit, study site, age and race/ethnicity
Three models were fit for each outcome: one with syndemic score, one with syndemic factor groups and one with all syndemi

in sexual risk behavior and STI over time require structural interventions that effectively address unemployment, low income and education, housing instability, and likelihood of incarceration for urban women. Policies that increase employment, raise minimum wages, secure affordable housing, provide opportunities for adult education and address over-policing in communities of color may reduce some of the negative association between structural factors and the sexual risk outcomes evaluated here.

Of note is the role of partner violence reported by one in three women in this study. Partner violence was significantly associated with all sexual risk behavior outcomes and a recent STI in the longitudinal analysis. Women experiencing partner violence may be less able to negotiate protected sex due to power dynamics.^{6,21} A study by El-Bassell et al.²¹ found that the relationship between partner violence and sexual risk was bidirectional, in that sexual risk behaviors were associated with subsequent partner violence as well as partner violence associated with subsequent sexual risk among women recruited from methadone maintenance clinics.²¹

The association of sexual risk with substance use, including heavy alcohol use is well documented.^{6,27} This study confirms the association of this individual level factor in this at-risk sample of women in three urban areas. Recent research among urban women has documented the syndemic nature of substance use, partner violence, depression and HIV risk,²⁷ with qualitative research describing how various syndemic factors may act as catalysts for each other.²⁸ Interrupting the proximal and interactive effects of these syndemic experiences on each other and sexual risk behavior outcomes is crucial. Although several interventions exist for substance using women at high risk for HIV and other STI, the Centers for Disease Control and Prevention no longer supports interventions such as SISTA, SHILE and VOICES/VOCES with training and other supports for CBOs and others (see here: <https://www.effectiveinterventions.org/en/HighImpactPrevention/Interventions/SIHLE.aspx>). The field is motivated therefore to develop novel interventions that blend biomedical and behavioral approaches and address structural barriers to optimal sexual health and well-being for urban women of color.

While it is encouraging that sexual risk and syndemic factors decreased from baseline to the first 6-month visit among the women in this study, limited change was observed thereafter. This phenomenon has been observed in many cohort and intervention studies^{29,30} and may be related to the risk reduction counseling delivered at each visit. Alternatively, the change early in follow-up may reflect “regression to the mean” given the high-risk eligibility criteria³¹ or a bias over time to report lower risk behaviors. We observed significantly higher odds of the reporting of any sexual risk behavior or recent STI with an increase in syndemic score, with structural factors (unemployment, housing instability, low education, lack of health insurance, incarceration), partner violence and substance use playing significant roles in sexual risk behaviors.

There are limitations to this study. The women were recruited for a study of HIV incidence using specific eligibility criteria to enroll at-risk women in three urban areas and thus do not represent all women in those areas. Thus, the prevalences of the syndemic factors are higher than in the general population and the correlations between factors are to be expected. Many of the questions asked about each syndemic factor were asked as dichotomous questions and thus more detailed exploration of the complexity of each factor, including dose, was not possible. The data frequencies did not allow us to separate different kinds of partner violence (sexual, physical, and emotional) with different types of partners (main and non-main). While the longitudinal design is advantageous, we cannot determine causality.

This study contributes to our understanding of factors contributing to HIV risk among US women by examining syndemic factors at multiple levels and their association with sexual risk. The significant role of structural factors highlights the challenge to designing effective HIV prevention interventions for at-risk urban women, who often experience multiple manifestations of extreme poverty at once. The findings highlight a group of women experiencing multiple poor social and health outcomes who need to be the focus of comprehensive combination HIV prevention strategies, including behavioral, structural and blended behavioral and biomedical approaches. With the release of recent clinical practice guidelines for pre-exposure prophylaxis use in the USA³², HIV prevention options have expanded for women at risk. To our knowledge, no interventions have been developed to promote and support PrEP uptake among women at risk. One of the challenges highlighted by these results is to provide the mechanisms and support for women facing multiple barriers to access the range of emerging HIV prevention strategies, in the context of significant and persistent structural risk factors.

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