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The effect of psychosocial syndemic production on 4-year HIV incidence and risk behavior in a large cohort of sexually active men who have sex with men

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Abstract

Background—Cross-sectional studies have suggested that co-occurring epidemics or "syndemics" of psychosocial health problems may accelerate HIV transmission among men who have sex with men (MSM) in the United States. We aimed to assess how five syndemic conditions (depressive symptoms, heavy alcohol use, stimulant use, polydrug use, and childhood sexual abuse) affected HIV incidence and sexual risk behavior over time.

Methods—Eligible men in a large, prospective cohort of sexually active, HIV-uninfected MSM completed HIV testing and behavioral surveys at baseline and every 6 months for 48 months. We examined interrelationships between psychosocial problems and whether these interactions increased the odds of HIV risk behaviors and risk of seroconversion over study follow-up.

Results—Among 4295 men, prevalence of psychosocial conditions was substantial at baseline and was positively associated with each other. We identified a statistically significant positive

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dose-response relationship between numbers of syndemic conditions and HIV seroconversion for all comparisons (with the greatest hazard among those with 4-5 conditions, aHR=8.69; 95% CI: 4.78-15.44). The number of syndemic conditions also predicted increased HIV related risk behaviors over time, which mediated the syndemic-HIV seroconversion association.

Conclusions—The accumulation of "syndemic" psychosocial problems predicted HIV-related sexual risk behaviors and seroconversion in a large sample of U.S. MSM. Given the high prevalence of syndemic conditions among MSM and the moderate effect sizes attained by traditional brief behavioral interventions to date, the HIV prevention agenda requires a shift toward improved assessment of psychosocial comorbidities and stronger integration with mental health and substance abuse treatment services.

Keywords

HIV; men who have sex with men; psychosocial conditions; prevention of sexual transmission; sexual behaviors

INTRODUCTION

Despite the development of empirically grounded behavioral interventions to reduce HIV transmission, incidence continues to increase among men who have sex with men (MSM) in the United States.[1] Most HIV prevention interventions focus on reducing specific sexual risk behaviors, yet MSM experience disproportionate burdens of depression, victimization, and distress[2-4] that promote sexual risk taking.[5-7] Several of these highly prevalent psychosocial problems also interact with substance abuse to produce additive or multiplicative effects on sexual risk.[8, 9] Over the past decade, research has suggested that these co-occurring epidemics among MSM may be intertwined, representing "syndemics" that accelerate HIV transmission.[10, 11]

The term "syndemic" was conceived to describe co-occurring and mutually reinforcing epidemics of substance abuse, violence, and AIDS ("SAVA") in poor urban communities.[12] While traditional epidemiological approaches conceptualize diseases as distinct entities, diseases often present in clusters and interact with each other to affect the health of particular groups in unique and detrimental ways.[13] Syndemic theory emphasizes how intertwined epidemics arise from adverse social conditions (e.g., poverty, social marginalization, political oppression) and interact to adversely affect health outcomes within disadvantaged communities. Recognizing the utility of this perspective in understanding HIV disparities, researchers have increasingly focused on identifying associations between co-occurring psychosocial problems and HIV risk taking among MSM and other sexual minority populations who are subject to high levels of social pressure, marginalization, and stress.[4, 11, 14]

While investigating syndemic factors in a cross-sectional sample of adult MSM, Stall and colleagues documented that greater numbers of psychosocial conditions were significantly associated with an increased odds of high risk sexual behaviors and already having HIV infection.[11] Mustanski and colleagues identified a similar phenomenon among younger MSM,[10] recently demonstrating the consequences of syndemics to be more severe for sexual

minority youth than those in the majority heterosexual population.[15] In addition to depression, victimization, and substance abuse, additional cross-sectional analyses have provided evidence that sexual compulsivity, stimulant use, intimate partner violence, stress, and childhood sexual abuse also interact to increase HIV risk among MSM.[5, 16-18] To improve the efficacy of behavioral interventions to prevent HIV among U.S. MSM, which have only achieved small to moderate effect sizes to date,[19, 20] a better understanding of how syndemics promote HIV risk among MSM over time could lead to the development of improved interventions that adequately target underlying, interacting psychosocial conditions and the broader social contexts from which they originate.

Despite this expanding evidence, research is needed to examine the syndemic production of HIV *longitudinally*. Thus, we drew from of large, prospective cohort of sexually active, HIV-uninfected MSM enrolled in a behavioral intervention in the United States to assess the interplay between multiple psychosocial health problems and determine the extent to which these syndemic conditions affected HIV seroconversion (becoming infected with HIV) over study follow-up and intervention efficacy. Based on previous work supporting the centrality of syndemics in heightening HIV risk among MSM,[5-7] we hypothesized that five specific psychosocial health conditions would interact over time (depressive symptoms, heavy alcohol use, stimulant use, polydrug use, and childhood sexual abuse) to increase sexual risk behavior and HIV seroconversion. We also sought to identify the most relevant syndemic psychosocial permutations with the overall goal of refining current HIV prevention intervention targets.

METHODS

Data originated from the EXPLORE study (HIVNET 015; previously detailed), a randomized controlled trial of a counseling intervention to prevent HIV acquisition among MSM in Boston, Chicago, Denver, New York, San Francisco and Seattle enrolled from January 1999 to February 2001.[21] Institutional review boards at each institution approved study procedures.

Study population

Eligible men were negative for HIV antibodies, ≥16 years old, and reported having anal intercourse with ≥ one man in the previous year. Men were excluded if they were in a mutually monogamous relationship for ≥ two years with a male partner known to be HIV seronegative. Recruitment included active, entertainment venue-based outreach, printed and electronic advertising, and referrals. Of 4862 men screened, 4296 were enrolled and randomized; 4295 were included in the final analysis.

Procedures

Participants completed HIV counseling and testing (via blood samples for HIV-antibody detection by ELISA) and behavioral surveys at baseline and every six months through 48 months. Reactive serum samples on a first test were retested; repeatedly reactive samples were confirmed by western-blot or immunofluorescence assays. Participants with positive

results at any visit were referred to appropriate services, and their participation in the study was discontinued.

Measures

HIV seroconversion and sexual risk behaviors—We assessed time from baseline to HIV seroconversion (or last visit with a negative HIV test) and sexual behaviors (past six months) with partners of presumed negative, positive, and unknown HIV serostatus. High risk sex (past 6 months) included 1) any unprotected insertive or receptive anal sex (UAS) with any partner, and 2) any unprotected insertive or receptive anal sex with partners of known-positive or unknown serostatus (herafter "serodiscordant UAS;" SDUAS).

Syndemic psychosocial conditions—Depressive symptoms were assessed using a 7-item Center for Epidemiologic Studies Depression (CES-D) scale measuring clinically significant distress as a marker for clinical depression (scores ≥13). Childhood sexual abuse was defined as having any sexual experience before age 13 with someone >5 years older, or between ages 13-17 with someone >10 years older and considering this experience to be sexual abuse; this was only measured at baseline. Heavy alcohol use was defined as having ≥4 drinks every day or ≥6 drinks on a typical day when drinking. Stimulant use was separated from other drugs due to its strong independent association with UAS and included any use of crack, cocaine, or amphetamines (past 6 months). Polydrug use was defined as using ≥3 nonprescription drugs excluding stimulants (marijuana, amyl nitrite "poppers," heroin, PCP, or other noninjectables; past 6 months). The syndemic measure was calculated as a count score based on the number of psychosocial conditions endorsed, resulting in scores ranging from 0-5. If participants were missing data on any of the items, the scale was not scored.

Baseline Covariates included age (categorized into 16-19, 20-25, 26-30, 31-35, 36-40, or >40 years), race (White, Black, Latino or other), highest education completed (high school or less, some college, college degree, or post-college), employment status (student, employed full-time, part-time, unemployed, or other), and annual income (<$6,000, $6,000-$11,999, $12,000-$29,999, $30,000-$59,999, ≥$60,000). Adjusted models included these covariates. Although the randomized trial did not find a statistically significant effect on risk of HIV infection between the intervention and control conditions,[22] adjusted models also controlled for study site location and randomization arm.

Statistical analysis

To describe the syndemic, we first examined frequencies and proportions of each psychosocial problem separately at baseline and over follow-up. In line with our syndemic framework, we also examined interrelationships between psychosocial problems at baseline via multiple multivariable logistic regression models of each psychosocial problem as the outcome. We then tested whether the syndemic measure changed over follow up using generalized estimating equations (GEE) with a multinomial link function for the nominal syndemic outcome measure.

To determine whether the number of psychosocial conditions increased seroconversion hazard over follow up, we fit a Cox proportional hazards regression model treating the syndemic measure as time-varying by using the value of the syndemic measure just prior to the event (i.e., HIV seroconversion or censoring). Because CSA was only measure at baseline, this measure was carried forward to each timepoint. We fit an unadjusted model and a model adjusting for baseline demographics, randomization arm, and study site. Using GEE with an unstructured covariance matrix, we also assessed whether the number of psychosocial conditions increased the odds of UAS and SDUAS over follow up. We also examined whether using only the baseline assessment of the syndemic measure impacted the results; however, because the measure did not change meaningfully or statistically over follow up, the regression results also did not differ meaningfully. As such, only the repeated measures analyses are presented.

Following the Baron and Kenny test of mediation, we examined whether sexual risk acted as a mediator between number of psychosocial conditions and HIV seroconversion. To determine whether having more psychosocial conditions modified the effect of the intervention on HIV seroconversion (the primary intervention outcome), we included the syndemic-by-treatment-condition interaction in a Cox model. Additionally, we included a syndemic-by-race/ethnicity interaction to determine if race/ethnicity modified the syndemic effect on HIV seroconversion.

To examine whether certain patterns of psychosocial problems played a larger role in the syndemic effect, we assessed differences in rates of seroconversion and population attributable fraction for 32 unique patterns of psychosocial problems. Since stimulant use was the most prevalent syndemic condition seen among the 32 unique patterns that we most attributable to HIV seroconversion, we also included stimulant use in our final, adjusted Cox regression model to examine the independent impact of both stimulant use and syndemic measure on hazard of HIV seroconversion. For this model, the syndemic measure was re-calculated to exclude stimulant use (range 0-4).

RESULTS

Among 4295 men, mean age was 34 years (SD: 9.4), 19.0% were ≤25 years of age, 72.5% were White, 15.2% were Latino, 6.5% were African-American, 35.8% had education less than a college degree, and 40.3% had an annual household income <$30,000, as previously described.[22] Psychosocial health conditions prevalent at baseline included depressive symptoms (47.3%), childhood sexual abuse (39.3%), stimulant use (25.1%), polydrug use (13.7%), and heavy alcohol use (10.5%; Table 1). There was not a statistically significant change in prevalence of the count of psychosocial health conditions over follow up, and the correlations for the count measure at each time point were high.

After adjusting for baseline covariates, every psychosocial condition at baseline was positively associated with all other psychosocial conditions with the exception of polydrug use, which was only significantly associated with stimulant use (Supplemental Table 1). At baseline, one quarter (24.5%) did not have any psychosocial health problems (Supplemental Table 2). Over one third (34.6%) had one, 24.0% had two, 10.3% had three, 4.3% had four,

and 0.7% had five. The distribution of these conditions did not change significantly over follow up (p=1.00).

Overall, 6.0% (n=259) seroconverted over follow up. Seroconversion rates were highest among those with more baseline psychosocial health problems: 15.2% of those with four or five conditions seroconverted, 10.0% of those with three, 7.7% of those with two, 5.1% of those with one, and 3.3% of those with no psychosocial health conditions.

The hazard of HIV seroconversion was highest for those with more psychosocial health problems over follow up, with a trend toward lower hazard with fewer conditions (Figure 1). Specifically, in both unadjusted and adjusted models, compared to those with no psychosocial health conditions, those with four or five conditions had 8.7 times the hazard of seroconverting over follow up (aHR=8.69; 95% CI: 4.78-15.44), those with three had 5.3 times the hazard of seroconverting (aHR=5.28; 95% CI: 3.31-8.44), those with two had 2.4 times the hazard (aHR=2.41; 95% CI: 1.55-3.76), and those with one condition had 1.7 times the hazard (aHR=1.68; 95% CI: 1.09-2.59; Table 2). A similar trend of increased risk for those with more psychosocial conditions was seen for the sexual risk behavior analysis as well (Table 2). Moreover, the sexual risk behaviors appeared to partially mediate the syndemic effect on HIV seroconversion; however while the risk of HIV was substantially attenuated at each level of psychosocial conditions, it remained high (e.g., when accounting for SDUA sex, aHR for 4/5 conditions vs. 0 conditions=5.06; 95% CI: 2.79-9.18).

The null effect of the EXPLORE intervention on HIV seroconversion was not modified by the syndemic measure (interaction p=0.722). With one exception, the control group was at higher risk of seroconverting within each strata of the syndemic measure (as were those who received the intervention within each strata of the syndemic measure compared to in the control condition with no syndemic conditions); however, these differences were not statistically different (Table 3). Additionally, the association between the syndemic measure and HIV seroconversion was not modified by race, indicating that while minority MSM have higher syndemic levels, the impact of the syndemic measure on HIV seroconversion does not differ by race/ethnicity.

To determine whether certain combinations of psychosocial conditions drove the syndemic effect, we examined all 32 (2^5) possible patterns of the psychosocial conditions (Table 4). We calculated population attributable hazard fractions (for this cohort) to assess the proportion of HIV seroconversion attributable to each distinct pattern of psychosocial conditions, assuming the association is causal. Using the overall seroconversion rate of 6.3% among those with non-missing syndemic data (n=4228), we classified 18 patterns as “high-risk” (seroconversion rate >6.3%) and 14 patterns as “low-risk” (seroconversion rate ≤6.3%). Of the 18 high-risk patterns, 15 included stimulant use. Of the 14 low-risk patterns, only one included stimulant use.

To assess whether stimulant use was driving the association between the syndemic measure and hazard of HIV seroconversion, we conducted post-hoc analyses including stimulant use and the syndemic measure (after removing stimulant use) simultaneously in an adjusted Cox regression model. Both stimulant use (aHR=2.31; 95% CI: 1.73-3.08) and the syndemic

variable (for three/four vs. none: aHR=3.84; 95% CI: 2.27-6.51; for two: aHR=2.07; 95% CI: 1.40-3.07; for one; aHR=1.38; 95% CI: 0.95-2.01) were associated with an increased hazard of HIV seroconversion. Thus, the syndemic effect was attenuated but remained large and had a larger independent effect on seroconversion than stimulant use alone.

DISCUSSION

This study demonstrates prospectively that the accumulation of "syndemic" or overlapping psychosocial problems predicts HIV seroconversion among U.S. MSM. In particular, we found that depressive symptoms, childhood sexual abuse, heavy alcohol use, stimulant use, and polydrug use interacted to produce additive effects on HIV-related sexual risk behaviors and seroconversion over 48 months of follow up, greatly extending prior cross-sectional research.[10, 11] We identified a dose-response relationship between increasing numbers of syndemic conditions and elevated HIV risk (e.g., those with four or five interacting psychosocial problems experienced 8.6 times the hazard of seroconversion while those with fewer interacting conditions experienced a lower hazard). Our study provides compelling evidence for the directionality of the effect of syndemics on increased HIV risk among MSM.

The preponderance of overlapping psychosocial problems identified in our large sample of MSM in six U.S. cities likely reflects the extent of mental health and substance abuse disparities in this population.[2-4] Despite 30 years of research on HIV risk among MSM, only recently have investigators begun to link these syndemic vulnerabilities, many of which can be traced back to social marginalization and disadvantage,[12] to the sexual health of MSM.[10, 11] That co-occurring psychosocial health problems persist into adulthood would contribute to HIV disparities among gay, bisexual, and other MSM is broadly consistent with Meyer's minority stress model.[4] This developmental model argues that early stressors associated with sexual minority status produce external and internal stress processes (e.g., antigay prejudice, discrimination, internalized homophobia, expectations of rejection) that contribute to mental health and substance use disorders later in life.[15] In support of this model, programs targeting discrimination and internalized homophobia among MSM have effectively reduced sexual risk.[23]

Conceptualizing the production of syndemic conditions in this way helps maintain focus on these important targets of the broader HIV prevention agenda, yet the social and structural causes of syndemics among MSM are typically out of the reach of traditional brief behavioral interventions.[19, 20] However, our study identified specific syndemic patterns that contribute to the highest levels of population attributable risk for seroconversion, providing specific intervention targets for prevention programs. MSM characterized by the higher risk patterns (e.g., stimulant users with depressive symptoms) may only benefit from sexual risk reduction counseling that is integrated into mental health and substance abuse treatment programs. While the "seek, test, treat and retain" strategy and other brief interventions have greater scalability and continue to play an important role in the prevention agenda, they may not be relevant for MSM experiencing multiple psychosocial comorbidities (approximately 40% of our sample). Thus, integrating sexual risk reduction counseling into other services and treatments may provide the greatest benefit for MSM experiencing the highest risk

syndemic patterns. Expanding the scope of HIV prevention in this way will, however, require embracing greater integration of services and a broader range of referrals. It will also require implementing improved assessment and diagnostic tools to identify those who require additional services.

The syndemic production of HIV suggests a need for more refined, comprehensive, clinical assessments of psychosocial comorbidities. Diagnostic assessments would allow greater specification of treatment targets to support referrals or linkage to care for individuals at heightened risk. Key syndemic indicators among MSM, including those identified in our study, are typically assessed via self-report. However, the use of clinician-administered diagnostic assessments would help identify those who meet diagnostic criteria for particular disorders or have characteristics of significant functional impairment (e.g., major depressive disorders, methamphetamine abuse/dependence). Similarly, our findings and previous research support the need to carefully differentiate between specific syndemic factors. In this sample, stimulant use is an important predictor of HIV seroconversion and is prevalent in the highest risk patterns of psychosocial conditions. Moreover, the influence of stimulant abuse on sexual compulsivity,[18] sexual assault, depression and general distress leading to sexual risk taking[10] is well documented. Notably, however, above and beyond stimulant use, the syndemic effect remained, suggesting that it is not stimulant use that is alone driving these findings. This further supports our study's distinction between heavy alcohol, stimulant, and polydrug use.

Refining syndemic assessments will allow identification of individuals at heightened risk as well as improved treatment targets for integrated prevention programs. Improved specification of adult mental health and substance abuse treatment targets may be particularly helpful for HIV prevention because there are established, efficacious behavioral and psychopharmacological treatments for many of these disorders (e.g., depression, anxiety, substance abuse).[24] For example, focusing prevention efforts on treating the persistent symptoms of posttraumatic stress in adulthood resulting from childhood sexual abuse (rather than just identifying the abuse) may yield significant improvements in reducing sexual risk taking. In other words, understanding the syndemic production of HIV risk from a developmental perspective helps clarify that the target for integrated HIV prevention programs should be the current dysfunction in adulthood rather than the distal developmental stressor of childhood sexual abuse itself. Emerging behavioral treatment technology has already yielded promising results by integrating behavioral treatments and sexual risk reduction counseling for MSM[25, 26] and other populations at heightened risk for HIV acquisition and transmission.[27, 28] Such a shift, informed by syndemic theory, will help interventions to consider but move beyond antecedent developmental vulnerabilities to more appropriately address the consequences, in this case for HIV seroconversion, of syndemic production.

There are limitations to consider with this study. First, our syndemic indicators were based upon self-report; thus, the extent of the impairment or distress associated with these measures is unknown. Recruitment for the intervention study occurred in large urban centers and we obtained a sample of relatively high SES, possibly preventing the generalizability of our findings to nonurban settings. Assessment of the higher-level, structural variables

highlighted in syndemic theory was also limited. Finally, as the focus of our study was on initially HIV-uninfected MSM, future research is also needed to characterize the syndemic production of HIV transmission among HIV-infected MSM, which may occur through direct influence on risk behaviors[29] or by interfering with viral load suppression via suboptimal treatment adherence and engagement in care.[30] Future syndemic research among HIV-infected MSM may also help identify appropriate targets for secondary prevention interventions.

Despite these limitations, this study is an important addition to the literature in that it establishes the prospective relationship between syndemic mental health and substance abuse problems and subsequent HIV sexual risk and seroconversion in a large sample of U.S. MSM. In addition to addressing the common social and structural causes of these co-occurring epidemics, the HIV prevention agenda will require greater integration of risk reduction counseling into existing mental health and substance abuse treatment services. Recent advances in behavioral health and prevention science research demonstrate that this approach is feasible; however, given the high prevalence of syndemic conditions among MSM and dramatically increased hazard of HIV seroconversion among those with multiple presenting syndemic conditions, now is the time to act. The efficacy of HIV prevention interventions will be enhanced by incorporating treatment components designed to address the specific presenting syndemic conditions among MSM.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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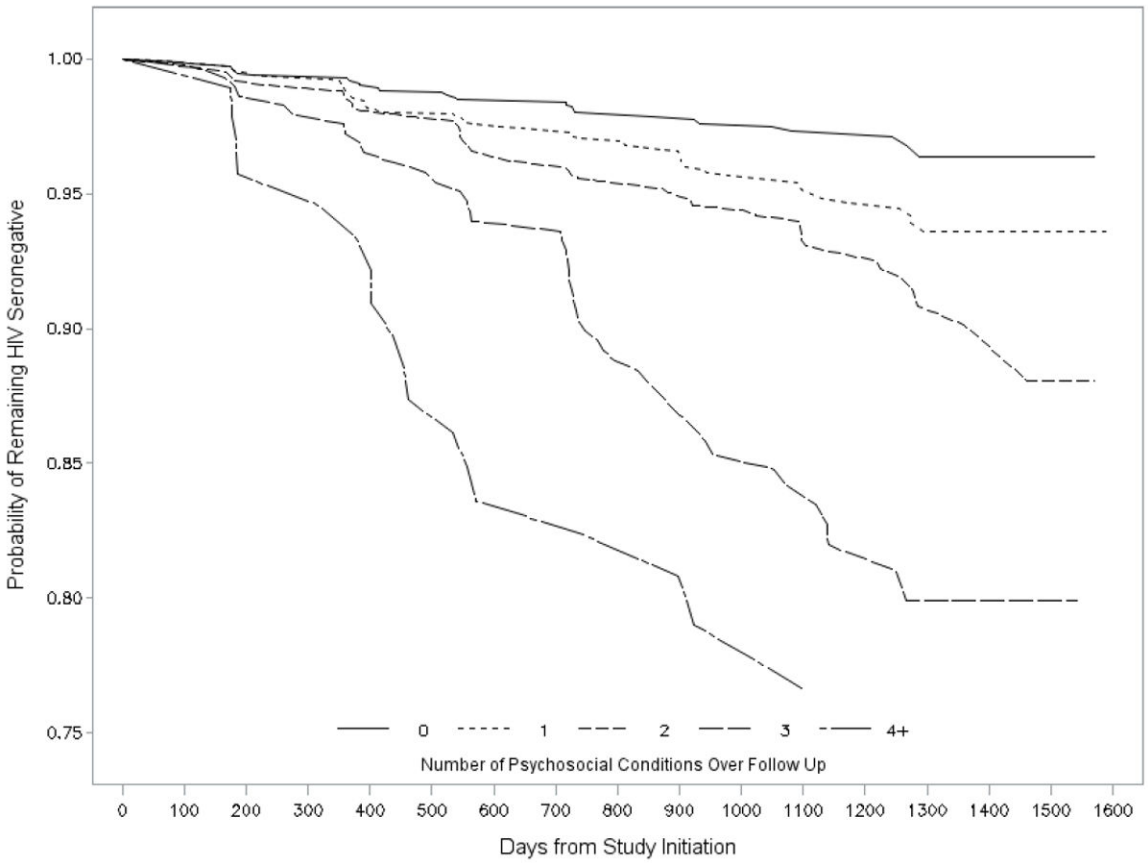

Figure 1.
Hazard of HIV seroconversion by syndemic condition.

Table 1

Frequencies and prevalence of individual psychosocial conditions at baseline and over follow-up

	Baseline	Month 6	Month 12	Month 18	Month 24	Month 30	Month 36	Month 42	Month 48
Number Attending Visit	**4295**	**3848**	**3719**	**3621**	**3559**	**3507**	**2541**	**1686**	**680**
Depressive Symptoms									
Missing	5 (0.1%)	40 (1.0%)	54 (1.5%)	58 (1.6%)	85 (2.4%)	122 (3.5%)	96 (3.8%)	66 (3.9%)	37 (5.4%)
No	2260 (52.6%)	2209 (57.4%)	2130 (57.3%)	2096 (57.9%)	2140 (60.1%)	2099 (59.9%)	1548 (60.9%)	1008 (59.8%)	393 (57.8%)
Yes	2030 (47.3%)	1599 (41.6%)	1535 (41.3%)	1467 (40.5%)	1334 (37.5%)	1286 (36.7%)	897 (35.3%)	612 (36.3%)	250 (36.8%)
Heavy Alcohol Use									
Missing	18 (0.4%)	68 (1.8%)	72 (1.9%)	72 (2.0%)	98 (2.8%)	129 (3.7%)	103 (4.1%)	69 (4.1%)	41 (6.0%)
No	3824 (89.0%)	3522 (91.5%)	3425 (92.1%)	3348 (92.5%)	3271 (91.9%)	3202 (91.3%)	2303 (90.6%)	1531 (90.8%)	606 (89.1%)
Yes	453 (10.5%)	258 (6.7%)	222 (6.0%)	201 (5.6%)	190 (5.3%)	176 (5.0%)	135 (5.3%)	86 (5.1%)	33 (4.9%)
Stimulant Use									
Missing	12 (0.3%)	44 (1.1%)	58 (1.6%)	59 (1.6%)	87 (2.4%)	125 (3.6%)	96 (3.8%)	66 (3.9%)	39 (5.7%)
No	3204 (74.6%)	2921 (75.9%)	2822 (75.9%)	2752 (76.0%)	2696 (75.8%)	2667 (76.0%)	1954 (76.9%)	1318 (78.2%)	526 (77.4%)
Yes	1079 (25.1%)	883 (22.9%)	839 (22.6%)	810 (22.4%)	776 (21.8%)	715 (20.4%)	491 (19.3%)	302 (17.9%)	115 (16.9%)
Polydrug Use									
Missing	8 (0.2%)	44 (1.1%)	58 (1.6%)	63 (1.7%)	91 (2.6%)	123 (3.5%)	96 (3.8%)	66 (3.9%)	39 (5.7%)
No	3698 (86.1%)	3350 (87.1%)	3255 (87.5%)	3175 (87.7%)	3116 (87.6%)	3123 (89.1%)	2254 (88.7%)	1511 (89.6%)	601 (88.4%)
Yes	589 (13.7%)	454 (11.8%)	406 (10.9%)	383 (10.6%)	352 (9.9%)	261 (7.4%)	191 (7.5%)	109 (6.5%)	40 (5.9%)
Childhood Sexual Abuse									
Missing	51 (1.2%)	45 (1.2%)	40 (1.1%)	38 (1.0%)	40 (1.1%)	38 (1.1%)	29 (1.1%)	22 (1.3%)	10 (1.5%)
No	2558 (59.6%)	2324 (60.4%)	2263 (60.8%)	2208 (61.0%)	2183 (61.3%)	2146 (61.2%)	1560 (61.4%)	990 (58.7%)	387 (56.9%)
Yes	1686 (39.3%)	1479 (38.4%)	1416 (38.1%)	1375 (38.0%)	1336 (37.5%)	1323 (37.7%)	952 (37.5%)	674 (40.0%)	283 (41.6%)

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Table 2

Associations between number of psychosocial conditions and time to HIV seroconversion, unprotected anal sex and serodiscordant unprotected anal sex over follow up.

	HIV Seroconversion		UA Sex		SDUA Sex	
Number of Psychosocial Conditions Over Follow Up	**Unadjusted Hazard Ratio (95% CI)**	**Adjusted Hazard Ratio[a] (95% CI)**	**Unadjusted Odds Ratio (95% CI)**	**Adjusted OddsRatio[a] (95% CI)**	**Unadjusted Odds Ratio (95% CI)**	**Adjusted OddsRatio[a] (95% CI)**
None	Reference	Reference	Reference	Reference	Reference	Reference
One	1.79 (1.17, 2.75)**	1.68 (1.09, 2.59)*	1.00 (0.90, 1.12)	1.04 (0.93, 1.16)	1.24 (1.11, 1.39)**	1.24 (1.11, 1.39)**
Two	2.63 (1.70, 4.07)***	2.41 (1.55, 3.76)**	1.42 (1.25, 1.60)***	1.49 (1.31, 1.70)***	1.68 (1.48, 1.90)***	1.69 (1.49, 1.91)***
Three	6.34 (4.02, 10.00)***	5.28 (3.31, 8.44)***	1.80 (1.50, 2.15)***	1.79 (1.49, 2.16)***	2.19 (1.84, 2.60)***	2.23 (1.87, 2.66)***
Four/Five	9.61 (5.43, 17.02)***	8.59 (4.78, 15.44)***	2.88 (2.03, 4.08)***	2.86 (2.02, 4.05)***	4.05 (3.09, 5.31)***	4.26 (3.24, 5.61)***

[a] Adjusted for age, race, education, household income, employment, site, and randomization arm.

* p<0.05

** p<0.01

*** p<0.0001

Table 3

Hazard of HIV seroconversion, by randomization arm and number of psychosocial conditions over follow up.

Number of Psychosocial Conditions Over Follow Up by Randomization Arm	N	Adjusted Hazard Ratio[a]	95% Confidence Interval	p-value
0 condition/Intervention arm	**518**	0.82	0.40, 1.70	0.598
0 condition/Control arm	**623**	1.00	-	-
1 condition/Intervention arm	**681**	1.43	0.81, 2.54	0.221
1 condition/Control arm	**675**	1.65	0.94, 2.90	0.083
2 conditions/Intervention arm	**412**	2.37	1.32, 4.23	0.004
2 conditions/Control arm	**438**	2.07	1.15, 3.73	0.015
3 conditions/Intervention arm	**144**	3.86	2.01, 7.42	<.0001
3 conditions/Control arm	**149**	5.79	3.19, 10.48	<.0001
4+ conditions/Intervention arm	**46**	9.27	4.35, 19.76	<.0001
4+ conditions/Control arm	**47**	11.26	4.90, 25.90	<.0001

[a] Adjusted for age, race, education, household income, employment, and site.

Table 4

Rate of HIV seroconversion over follow up by pattern of psychosocial conditions at baseline and population attributable hazard fraction (PAHF), ordered by rate of seroconversion

Patterns of Psychosocial Conditions at Baseline	% HIV Seroconverted	Total N	PAHF	95% CI	p-value
Polydrug Use/CSA	0	24	--		
Heavy Alcohol/Polydrug	0	3	--		
Depressive Symptoms/Polydrug Use	0	24	--		
Heavy Alcohol/CSA/Polydrug Use	0	3	--		
Depressive Symptoms/Heavy Alcohol/Polydrug Use	0	3	--		
Depressive Symptoms/Heavy Alcohol/Polydrug Use/CSA	0	5	--		
None	3.33	1020	Ref.		
Polydrug Use	3.92	51	0.001	-0.010, 0.012	0.838
Depressive Symptoms	4.52	686	0.031	-0.022, 0.082	0.247
Heavy Alcohol	5.08	59	0.004	-0.009, 0.018	0.525
Stimulant Use/CSA/Heavy Alcohol	5.26	19	0.001	-0.007, 0.009	0.740
Depressive Symptoms/CSA/Polydrug Use	5.26	19	0.001	-0.006, 0.009	0.731
CSA	5.40	500	0.040	-0.006, 0.084	0.088
Depressive Symptoms/CSA	6.12	490	0.055	0.007, 0.100	0.024*
Stimulant Use/CSA/Depressive Symptoms	7.48	107	0.017	-0.005, 0.039	0.123
Stimulant Use	7.69	143	0.025	-0.001, 0.050	0.063
CSA/Heavy Alcohol	8.82	34	0.007	-0.006, 0.021	0.273
Stimulant Use/Heavy Alcohol/Depressive Symptoms	8.82	34	0.008	-0.005, 0.021	0.231
Stimulant Use/CSA	9.01	111	0.025	0.001, 0.049	0.045*
Stimulant Use/Heavy Alcohol/Polydrug Use	9.09	11	0.003	-0.005, 0.010	0.527
Depressive Symptoms/Heavy Alcohol	9.26	54	0.013	-0.004, 0.030	0.135
Depressive Symptoms/Heavy Alcohol/**Stimulant Use**/CSA	10.00	40	0.011	-0.004, 0.026	0.160
Depressive Symptoms/Heavy Alcohol/**Stimulant Use**/CSA/Polydrug Use	10.00	30	0.008	-0.005, 0.022	0.211
Depressive Symptoms/**Stimulant Use**	10.83	120	0.036	0.009, 0.063	0.010*
Stimulant Use/Polydrug Use	11.22	98	0.031	0.006, 0.056	0.016*
Depressive Symptoms/CSA/Heavy Alcohol	11.94	67	0.023	0.002, 0.045	0.035*
Stimulant Use/CSA/Polydrug Use	12.24	49	0.017	-0.001, 0.036	0.070

Patterns of Psychosocial Conditions at Baseline	% HIV Seroconverted	Total N	PAHF	95% CI	p-value
Stimulant Use/Depressive Symptoms/Polydrug Use	12.84	109	0.042	0.013, 0.069	0.005**
Heavy Alcohol/**Stimulant Use**	16.67	18	0.009	-0.004, 0.022	0.156
Depressive Symptoms/Heavy Alcohol/**Stimulant Use**/Polydrug Use	16.67	24	0.013	-0.002, 0.028	0.095
Depressive Symptoms/**Stimulant Use**/Polydrug Use/CSA	18.39	87	0.053	0.023, 0.082	0.001**
Heavy Alcohol/**Stimulant Use**/Polydrug Use/CSA	25.00	12	0.011	-0.003, 0.024	0.116

Note: Light shading indicates “low-risk” patterns (i.e., the rate of seroconversion was less than the overall rate, 6.3%). Dark shading indicates “high-risk” patterns (i.e., the rate of seroconversion was greater than the overall rate).

PAHF=Population Attributable Hazard Fraction, or the fraction of HIV seroconversion attributable to each distinct pattern of the psychosocial conditions in the cohort, assuming the association is causal.

* p<0.05

** p<0.01