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# Gender and Age Patterns in HSV-2 and HIV Infection Among Non-Injecting Drug Users in New York City

Don C. Des Jarlais, PhD\*, Kamyar Arasteh, PhD\*, Courtney McKnight, MPH\*, David Perlman, MD\*, Holly Hagan, PhD†, Salaam Semaan, DrPH‡, and Samuel R. Friedman, PhD§ \*Beth Israel Medical Center, Baron Edmond de Rothschild Chemical Dependency Institute, New York, NY

<sup>†</sup>New York University College of Nursing, New York, NY

<sup>‡</sup>Centers for Disease Control and Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Atlanta, GA

§National Development and Research Institutes, The Institute for AIDS Research, New York, NY

#### Abstract

**Objective**—To examine prevalence of and associations between herpes simplex virus type 2 (HSV-2) infection and HIV infection among never-injecting heroin and cocaine drug users (NIDUs) in New York City.

**Methods**—Subjects were recruited from patients entering the Beth Israel drug detoxification program. Informed consent was obtained, a structured questionnaire including demographics, drug use history, and sexual risk behavior was administered, and a blood sample was collected for HIV and HSV-2 antibody testing.

**Results**—A total of 1418 subjects who had never (lifetime) injected drugs (NIDUs) were recruited between July 2005 through June 2009. Subjects were primarily male (76%), and black (67%) or Hispanic (25%), reported recent crack cocaine use (74%), and had a mean age of 42 years. Eleven percent of males reported male-with-male sexual (MSM) behavior. The prevalence of both viruses was high: for HSV-2, 61% among the total sample, 50% among non-MSM males, 85% among females, and 72% among MSM; for HIV, 16% among the total sample, 12% among non-MSM males, 20% among females, and 46% among MSM. HSV-2 was associated with HIV (OR = 3.2, 95% CI: 2.3–4.5; PR = 2.7, 95% CI: 2.0–3.7). Analyses by gender and age groups indicated different patterns in mono- and coinfection for the 2 viruses.

**Discussion**—HSV-2 and HIV rates among these NIDUs are comparable with rates in sub-Saharan Africa. Additional prevention programs, tailored to gender and age groups, are urgently needed. New platforms for providing services to NIDUs are also needed.

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Correspondence: Don C. Des Jarlais, PhD, Beth Israel Medical Center, 160 Water St, 24th Floor, New York, NY 10038. dcdesjarla@aol.com..

The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

There is considerable biologic and epidemiologic evidence that herpes simplex virus type 2 (HSV-2) infection is a cofactor for both acquiring and transmitting HIV. Two metaanalyses and a recent qualitative review have concluded that prevalent HSV-2 infection is associated with an increased likelihood of acquiring HIV by a factor of 2 to 3. <sup>1-3</sup> At the biologic level, HSV-2 may create lesions that may serve as entry portals for HIV while simultaneously recruiting target cells (dendritic and CD4+ cells) for HIV infection to the genital mucosa. HSV-2 infection also increases HIV RNA in genital secretions and may also increase transmission HIV.<sup>4</sup>

Most research on the relationships between HSV-2 and HIV has been conducted in sub-Saharan Africa, and it has been estimated that HSV-2 may account for 35% to 48% of HIV infections in various sub-Saharan African cities.<sup>5</sup> There are also populations in the United States, particularly noninjecting heroin and cocaine users, for which HSV-2 infection may be strongly related to HIV infection. There have been a moderate number of studies of HSV-2 and HIV among heroin and cocaine users. <sup>1,4,6,7</sup> In a review of the limited number of studies with drug users, the prevalence of HSV-2 among drug users ranged from 38% to 61%. 8,9 This reported prevalence of HSV-2 among drug users is much higher than the prevalence of 17% reported for the general population. <sup>10</sup> These studies tend to show positive associations between HSV-2 and HIV prevalence, but it is extremely difficult to generalize across the studies. The studies vary not only in geographic location (with associated variation in HIV prevalence), but in subject recruitment methods, whether injecting and noninjecting drug users were included in the sample (often without separate analyses), whether types of noninjecting drug use other than crack cocaine were included in the sample, and in age restrictions for the sample. 11 Given the evidence for elevated rates of HSV-2 among drug users, and the linkages of HSV-2 to sexual transmission of HIV, it is important to develop a better understanding of the relationships between HSV-2 and HIV among both injecting and noninjecting drug users.

In this report, we examine prevalence of HSV-2 and HIV among never-injecting heroin and cocaine users (NIDUs) recruited from a large drug detoxification program in New York City. We specifically examine the relationships between the 2 viruses by gender and age to provide insight into the likely timing of acquisition of the viruses.

## **MATERIALS AND METHODS**

The data reported here are derived from ongoing data collection from drug users entering the Beth Israel Medical Center drug detoxification program in New York City. The methods for this "Risk Factors" Study have been previously described in detail, <sup>12,13</sup> and so only a summary will be presented here. The Beth Israel detoxification program serves the city as a whole, and approximately half of its patients live in Manhattan, one-quarter in Brooklyn, one-fifth in the Bronx, and the remainder (i.e., 5%) live elsewhere. Patients enter the program voluntarily.

Both injecting and noninjecting drug users entering the detoxification program are eligible to participate in the study. The present analyses include only persons who reported that they have never injected illicit drugs. Hospital records and the questionnaire results are checked

for consistency on route of drug administration and arms are examined for evidence of injecting.

Research staff visited the general admission wards of the program in a preset order and examined all intake records of a specific ward to construct lists of patients admitted within the prior 3 days. All of the patients on the list for the specific ward were then asked to participate in the study. Among patients approached by our interviewers, willingness to participate was more than 95%. After all the patients admitted to a specific ward in the 3-day period had been asked to participate and interviews had been conducted among those who agreed to participate, the interviewer moved to the next ward in the preset order. Because there is no relationship between assigning patients to wards and the order that the staff rotate through the wards, these procedures should produce an unbiased sample of persons entering the detoxification program.

A structured questionnaire covering demographics, drug use, sexual risk behavior, and use of HIV prevention services was administered by a trained interviewer. Participants were included in the analyses presented here if they had reported that they had never injected illicit drugs. The self-report of never injecting was checked against the detoxification program records, and the subject's arms were examined for any evidence of drug injecting. Most HIV risk behavior questions referred to the 6 months before the interview. Male-withmale sexual (MSM) behavior was assessed by asking males about sex with other males in the 5 years before the interview.

After completing the interview, the participant was seen by an HIV counselor for pretest counseling and specimen collection. HIV testing was conducted at the New York City Department of Health Laboratory by using a commercial, enzyme-linked, immunosorbent assays test with Western blot confirmation (BioRad Genetic Systems HIV-1–2 + 0 EIA and HIV-1 Western Blot, BioRad Laboratories, Hercules, CA). HSV-2 testing was performed by BioReference Laboratories using the Focus HerpeSelect 1 and 2 enzyme linked immunosorbent assay (ELISA). We used an optical density value of 1.1 for classifying a subject as HSV-2-seropostive. We also examined the distribution of the optical density scores. A total of 10% of subjects had optical density values between 1.1 and 3.5, and were potentially false positives. Removal of these subjects from the analyses would reduce the HSV-2 prevalence by approximately 4%, but would not change any of the relationships between HSV-2 and HIV.

Individuals who enter the detoxification program multiple times are permitted to participate in the study multiple times, although not more than once per year. For the analyses reported here, we used only 1 interview by subject, with a randomly selected interview from subjects with multiple interviews.

The Stata statistical (StataCorp, College Station, TX) programs and SAS software, version 9 (SAS Institute, Inc., Carey, NC) were used for statistical analyses. We report both odds ratios and prevalence ratios—odds ratios because they are the more commonly used measure of association and prevalence ratios as they provide a more intuitive interpretation for events

with high frequency of occurrence. Both the odds ratios and the prevalence ratios are for HIV prevalence by HSV-2 status.

The study was approved by the Beth Israel Medical Center Institutional Review Board.

#### **RESULTS**

Table 1 presents selected demographic characteristics and recent (past 6 month) drug use behaviors of the 1418 subjects recruited into the study between July 2005 and June 2009. The subjects were predominantly male and ethnic minority group members. Smoking crack cocaine was the drug reported by a large majority (74%), but substantial percentages also reported intranasal cocaine and heroin use. Subjects could report using more than 1 drug in the 6 months before the interview. The average age was 42 years.

HSV-2 and HIV prevalence by demographic and drug use characteristics are presented in Table 2. There were statistically significant differences by gender/MSM behavior in seroprevalence of both viruses (with non-MSM males lowest), by race/ethnicity, and with whites having the lowest and blacks having the highest prevalence for both viruses. There was a statistically significant increasing gradient for HSV-2 prevalence by age; the youngest age group did have the lowest HIV prevalence, but there was no statistically significant gradient by age for HIV prevalence. Subjects who reported recent (past 6 months) use of crack cocaine had significantly higher prevalence for both viruses. For the sample as a whole, there was a strong relationship between HSV-2 and HIV, odds ratio = 3.2, 95% CI: 2.3 to 4.5 (PR = 2.7, 95% CI: 2.0–3.7).

We examined mono-infections (HSV-2 only and HIV only) and coinfection (both HIV and HSV-2) by 10-year age groups to identify potential patterns in acquisition of the 2 viruses. In interpreting the infections by age group, it is important to note that some HIVseropositive NIDUs in the older age groups may have been lost to active noninjecting drug use because of disability or death, or cessation of drug use. As HSV-2 infection may increase plasma HIV, there is the likelihood that coinfected (both HIV and HSV-2) persons might be even more likely to be lost to disability or death. Additionally, some noninjecting drug users will have begun injecting, possibly after infection with HSV-2 and/or HIV, and no longer be eligible for this "never injected" sample. Results for the total sample are presented in Figure 1. There was a significant decline in the percentages of subjects with neither infection with increasing age, a significant increase in the percentages of subjects with HSV-2 only and with coinfection, and a significant decline in the percentages of subjects with HIV only (all P < 0.01 by Cochran-Armitage tests). In a logistic regression analysis, the interaction between age as continuous variable and HSV-2-seropositive status was a highly significant predictor of HIV-seropositive status (P < 0.01, data not presented, available from first author). We considered a full multivariate analysis of HIV serostatus as a function of HSV-2 serostatus and the other variables shown in Table 3, but the extreme distribution of HSV-2 and HIV among the females precluded such modeling.

There were, however, important differences in the agerelated patterns of HSV-2 and HIV infection by gender/MSM behavior. Figures 2A–C show these results for female NIDUs, for

non-MSM male NIDUs (males who did not report sexual activity with another male in the 5 years before the interview), and for MSM NIDUs (who did report sexual intercourse with another male in the 5 years before the interview). First, we must note that there were highly significant differences in the percentages of HIV-seropositive NIDUs who were also HSV-2 seropositive by gender/MSM behavior; among the female NIDUs, 67 of 69 (97%) of the HIV-seropositives were also HSV-2-seropositive, among the MSM NIDUs, 44 of 52 (85%) of the HIV-seropositives were also HSV-2-seropositive, and among the non-MSM male NIDUs, 77 of 112 (69%) of the HIV-seropositives were also HSV-2-seropositive were also HSV-2-seropositive (P < 0.01 by  $\chi^2$  test).

Among the female NIDUs (Fig. 2A), there was a very strong association between HSV-2 and HIV, OR = 7.1, 95% CI: 1.7 to 30.0 (PR = 5.7, 95% CI: 1.5–22.6). Infection with HIV without infection with HSV-2 was rare; only 2 of 69 (3%) of the HIV-seropositive female NIDUs were HSV-2-seronegative, so that it was not possible to examine differences in HSV-2 with HIV by age group among the female NIDUs. There were only a moderate number (16) of female NIDUs in the youngest age group, of whom a majority (75%) was HSV-2-seropositive, and none were HIV-seropositive. With increasing age, the percentages that were coinfected with both HSV-2 and HIV increased significantly (P < 0.05 by Cochran-Armitage test). Among the oldest age group, 93% of the females were seropositive for either HSV-2 alone (69%) or for both HSV-2 and HIV (24%).

There was a statistically significant relationship between HSV-2 and HIV among the non-MSM male NIDUs, OR = 2.4, 95% CI: 1.6 to 3.6 (PR = 2.2, 95% CI: 1.5–3.2). As shown in Figure 2B, a moderate percentage of the non-MSM male HIV-seropositive NIDUs was HSV-2-seronegative (35/112, 31%). Among the youngest group of non-MSM male NIDUs, a moderate percentage (22%) was HSV-2-seropositive and 10% were HIV-seropositive, but none were infected with both viruses. HSV-2 infection increased with age among the non-MSM male NIDUs, and the percentages who were infected with HIV only and who were infected with neither virus declined with increasing age (all P < 0.05 by Cochran-Armitage tests).

There were 114 male subjects who reported engaging in sex with another male in the 5 years before the interview. This number did not permit assessing infections by 10-year age groups, so we divided the MSM sample in <40 and 40 years (Fig. 2C). The MSM NIDUs had a high prevalence of HSV-2, 72% overall, 56% among those less than age 40, and 81% among those aged 40 or more. They also had a very high rate of HIV prevalence–46% overall, 39% among those less than age 40, and 49% among those aged 40 or more. The percentage of the MSM NIDUs with no infections was significantly lower among the older subjects (P < 0.05 by  $\chi^2$  test). HSV-2 was strongly associated with HIV, OR = 3.5, 95% CI: 1.4 to 8.6 (PR = 2.2, 95% CI: 1.1–4.0).

We examined recent sexual risk behaviors by HSV-2 and HIV serostatus for the non-MSM male and female NIDUs. Sexual behavior refers to vaginal or anal intercourse with a partner of the opposite sex in the 6 months before the interview A separate report is being prepared for the MSM NIDUs (Table 3). Sex with a "client" refers to receiving money or drugs for sex (use of the term "client" does not imply that the person providing the sex was in a

position to require that condoms be used, particularly as the provider may have been in a state of drug craving or received a higher price for sex without a condom.). Because the great majority of the HSV-2- and HIV-seropositives were likely to have been infected well before the 6 months before the interview, the sexual risk behavior data should not be used to identify how various individuals became infected. Rather, these sexual risk behavior data provide information about the risks for acquiring infection among persons who are seronegative and transmitting infections among persons who are seropositive.

Because there were only 2 females who were HIV-seropositive without being HSV-2-seropositive, we did not calculate percentages for these 2 female subjects nor include them in the comparisons of risk behavior by infection status for females. Among both non-MSM males and females, fewer HIV-seropositives reported unprotected vaginal intercourse with any sexual partner and with primary sexual partners than did HIV-seronegatives. The only other statistically significant difference was that HSV-2 mono-infected females were more likely to report having multiple partners (which would put them at greater risk for acquiring HIV). The lower rates of risk behavior among the HIV-seropositives are likely due to the great majority of the HIV-seropositives knowing their status, because 87% of the HIV-seropositives reported that they had been tested for HIV before participating in the study.

In general, substantial percentages of subjects reported sexual risk behavior in the 6 months before the interview, with approximately three-quarters being sexually active, approximately one-quarter having multiple partners, more than half having unprotected sex with at least 1 partner, and approximately half having unprotected sex with a primary partner. The percentages reporting unprotected sex with casual partners and with clients were lower, but far from negligible.

# **DISCUSSION**

This is a cross-sectional study, and we do not have data on the behavior of the subjects before either HSV-2 or HIV infection. Sexual risk behaviors, sexual network patterns, and HIV prevalence among NIDUs in New York are likely to have changed substantially over the several decades in which these subjects were at risk for acquiring HSV-2 and HIV. Finally, it is likely that many persons were lost to the active noninjecting drug use population because of disability or death, transitioning to injecting drug use, or cessation of drug use. Despite these limitations, there would appear to be a few working inferences that can be drawn from the patterns in the data in Figures 1 and 2A–C. First, HSV-2 prevalence was higher than HIV prevalence among all gender/MSM behavior groups and in all age groups, suggesting that these NIDUs are likely to have acquired HSV-2 before HIV. Second, lack of infection is significantly less common, and coinfection is significantly more common in the older age groups, suggesting that these NIDUs continue sexual risk behaviors and acquire new infections over time.

These inferences would apply most clearly to the female NIDUs, where HSV-2 prevalence was high among all age groups, all but 2 of the 69 HIV seropositives were also HSV-2 seropositive, and more than 90% in the oldest age group had at least 1 of the 2 infections. The relatively high HSV-2 prevalence (12/16, 75%) among the under age 30 females

suggests efforts to prevent HSV-2 infection would need to begin at relatively young ages. It may be too late to prevent HSV-2 infection for many of the female NIDUs if prevention efforts do not begin until they seek treatment for drug-related problems.

The data for the young non-MSM male NIDUs suggest that this group would be most likely to have acquired HIV without having acquired HSV-2 first. It would be useful to conduct further research to determine the specific behaviors and sexual network factors associated with acquiring HIV among the younger non-MSM male NIDUs. One concern is that the older non-MSM male NIDUs are more likely to be dually infected with both HSV-2 and HIV compared with the younger non-MSM male NIDUs. If a HIV mono-infected male acquires HSV-2 from a sexual partner, he may be particularly likely to transmit HIV to this partner.

HSV-2 prevalence was high (72%) and HIV prevalence (46%) was very high among the MSM-NIDUs. Given the modest percentage of MSM NIDUs who were seropositive for HIV alone, it would seem that the majority of dually infected HIV seropositive MSM-NIDUs acquire HSV-2 before acquiring HIV, though the MSM-NIDUs as a group seem to be intermediate between the female and non-MSM male NIDUs in their patterns of coinfection with the 2 viruses.

Female-male differences in the strength of the associations between HVS-2 and HIV have been noted in previous studies of heroin and cocaine users. In the data reported here, females have higher HSV-2 prevalence than non-MSM males (85% vs. 50%), higher HIV prevalence than non-MSM males (20% vs. 12%), and the percentage of HIV seropositives who were also HSV-2 seropositives was also higher among the females than among the non-MSM males (97% vs. 69%). Our analyses by age categories further suggest that the females are acquiring HSV-2 at relatively earlier ages than the non-MSM males. The MSM males had an HSV-2 prevalence intermediate between the non-MSM males and the females, but an HIV prevalence that was higher than the prevalence for either the non-MSM males or the females.

As noted in the introduction, there have been few previous studies of HSV-2 and HIV among heroin and cocaine users, and it is very difficult to generalize findings from these studies because of the many differences in the research methods, particularly in subject recruitment procedures. In the current study, we found differences in the prevalence of HSV-2 and HIV by gender/MSM behavior, by race/ethnicity, a statistically significant HSV-2 by age interaction for HIV prevalence, and statistically significantly lower rates of risk behaviors among the HIV-seropositives. The complexity of these findings should be taken as a strong caution against simple models linking risk behavior, HSV-2 transmission, and HIV transmission for noninjecting drug users.

Several limitations of the current study should be noted. We did not have information on the drug use, age, race/ethnicity, or the HSV-2 or the HIV status of the current or past sexual partners of the subjects. The sexual partners may have included injecting drug users and nondrug users, as well as other noninjecting drug users.

The data on drug use and sexual behavior were obtained through self-report. Not having injected drugs was verified against hospital records and physical examination of arms during blood collection. Although some of the subjects may have injected and not reported this behavior, it is very unlikely that they would have had extensive injecting histories. Any subjects who might have injected and acquired HIV through sharing injection equipment would tend to bias the data toward a null hypothesis of no association between HSV-2 and HIV.

We used "last 5 years" as the period for inquiring about MSM behavior to have a relatively long period without including adolescent experimentation. It is thus possible that some MSM-IDUs were misclassified because of behaviorally significant MSM behavior before the last 5 years or because of misreporting. It would not seem likely, however, that such misclassification would be large enough to affect the results.

All of the subjects in this study were recruited from a single drug detoxification program in New York City. In a previous study, however, we found almost identical HIV prevalence among NIDUs from this detoxification program and NIDUs recruited in the community (using respondent driven sampling).<sup>14</sup>

The major limitation of the current study is its crosssectional design. We used age differences to make inferences about the likely patterns in acquiring HSV-2 and HIV among our subjects rather than actually observing incident infections with HSV-2 and HIV among NIDUs in New York City. The cross-sectional design may be particularly subjected to loss of HIV-seropositives among the older age groups as a result of death or disability. As noninjecting drug users age, they may have also ceased drug use or transitioned to injecting drug use, and thus may not be eligible as "current drug users who had never injected." We did, however, have 859 HSV-2-seropositives and 233 HIV-seropositives among our subjects. A longitudinal study that would have included these numbers of HSV-2 and HIV seroconversions would be logistically complex, require very extensive resources, and good research ethics would require providing treatment for HIV and HSV-2.

The prevalence of HSV-2 and of HIV among these noninjecting drug users are equal to or greater than the prevalence of HSV-2 and HIV in many parts of sub-Saharan Africa, <sup>2,5</sup> and must be seen as a failure of STD and HIV prevention in the United States. Indeed, an appropriately scaled version of the President's Emergency Program for AIDS Relief (PEPFAR) Southern Africa Prevention Initiative would be justified for these noninjecting drug users.

Recent trials of suppressive therapy for HSV-2 have shown no protective effect against either HIV acquisition <sup>15,16</sup> or transmission. <sup>15</sup> It seems that the standard dosages of the HSV-2-suppressant medication were not sufficient to provide protection against HIV transmission. Whether a biomedical intervention can be developed that reduces HIV acquisition among HSV-2-seropositives or reduces HIV transmission among coinfected individuals remains to be determined.

To our knowledge, there has been no research on preventing HSV-2 infection among noninjecting (or among injecting) drug users in the United States. Preventing HSV-2 among

the female NIDUs and among the black NIDUs in our sample would clearly be challenging, but given the great need, this should be considered an important question for future research. We would strongly recommend that future research on reducing HSV-2-related HIV transmission include US NIDUs as part of the research sample.

At present, there is no service platform for providing continuing HIV prevention and other health services for noninjecting cocaine users (either crack smokers or intranasal and cocaine users). There are syringe exchange programs that provide continuing services for injecting drug users, and methadone maintenance programs that provide continuing services for heroin users.

The statistically significant differences in the patterns of HSV-2 and HIV between the non-MSM NIDUs and the female NIDUs suggest that it would be important to provide prevention services tailored to the needs of each gender. For example, interventions that taught females how to negotiate greater condom use, including for both male and female condoms, might be helpful. Providing female condoms at no cost could be part of such interventions. HSV-2 prevention programs for female NIDUs should also begin at relatively young ages, probably before these females sought drug abuse treatment. For male NIDUs, circumcision might be considered as a potentially effective HIV prevention intervention, and behavioral interventions that stressed how acquiring HSV-2 might interfere with primary relationships might be developed. All such programs, however, would need to be rigorously evaluated, preferably with HSV-2 or HIV incidence as an outcome measure.

HIV prevalence among the MSM NIDUs was quite high at 46%. More than one-third (36%) of the MSM NIDUs reported sex with women in the 6 months before the interview; hence, there is a clear potential for HIV transmission between these MSM NIDUs and women. Special HIV prevention programs are urgently needed to reduce HIV acquisition among and transmission from the MSM NIDUs.

Interventions that teach basic information about HSV-2, counsel and test for HSV-2, and use knowledge of HSV-2 status to effectively reduce risk behavior are clearly needed for NIDUs. We are currently working on the development of such interventions.

A total of 87% percent of the HIV-seropositive subjects reported that they had previously been tested for HIV and knew that they were seropositive (though only 49% were currently receiving antiretroviral treatment). The HIV-seropositive subjects did report substantially less unsafe sex with their primary partners than did HIV-seronegative subjects. There is evidence that "prevention for positives" can be effective among injecting drug users. <sup>17</sup> Identifying HIV-seropositive NIDUs and providing them with antiretroviral treatment may be the most readyto-implement intervention to reduce sexual transmission of HIV among NIDUs. This would, however, require service platforms for regular HIV testing of NIDUs and services to ensure that continuing noninjecting drug use did not create problems with adherence to HIV antiretroviral therapy.

Finally, we need better surveillance of HSV-2 and HIV infection among noninjecting drug users. At present, the US national HIV surveillance system does not capture either noninjecting drug use or HSV-2-related HIV infections. Without a monitoring system for

HIV infection among NIDUs, we will neither be able to target appropriate prevention activities nor evaluate the community-level effectiveness of such activities.

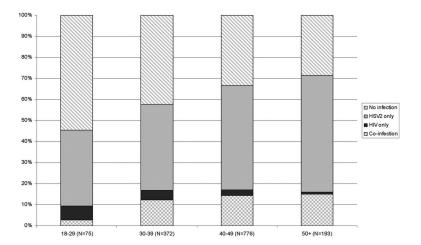
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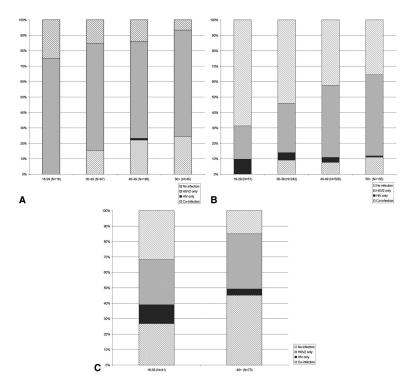
#### REFERENCES

- Freeman E, Weiss H, Glynn J, et al. Herpes simplex virus 2 infection increases HIV acquisition in men and women: Systematic review and meta-analysis of longitudinal studies. AIDS. 2006; 20:73– 83. [PubMed: 16327322]
- Tobian A, Quinn T. Herpes simplex virus type 2 and syphilis infections with HIV: An evolving synergy in transmission and prevention. Curr Opin HIV AIDS. 2009; 4:294–299. [PubMed: 19532067]
- 3. Wald A, Link K. Risk of human immunodeficiency virus infection in herpes simplex virus type 2-seropositive persons: A metaanalysis. J Infect Dis. 2002; 185:45–52. [PubMed: 11756980]
- 4. Van de Perre P, Segondy M, Foulongne V, et al. Herpes simplex virus and HIV-1: Deciphering viral synergy. Lancet Infect Dis. 2008; 8:490–497. [PubMed: 18652995]
- 5. Freeman E, Orroth K, White R, et al. Proportion of new HIV infections attributable to herpes simplex 2 increases over time: Simulations of the changing role of sexually transmitted infections in sub-Saharan African HIV epidemics. Sex Transm Infect. 2007; 83:i17–i24. [PubMed: 17405782]
- 6. Plitt S, Sherman S, Strathdee S, et al. Herpes simplex virus 2 and syphilis among drug users in Baltimore, Maryland. Sex Transm Infect. 2005; 81:248–253. [PubMed: 15923296]
- Wald A. Synergistic interactions between herpes simplex virus type-2 and human immunodeficiency virus epidemics. Herpes. 2004; 11:70–76. [PubMed: 15960904]
- 8. Des Jarlais, D.; Semaan, S.; Holmes, K.; Sparling, P.; Stamm, W., et al. McGraw Hill; New York, NY: 2008. HIV and other sexually transmitted infections in injection drug users and crack cocaine smokers; Sexually Transmitted Diseases; p. 237-255.
- Semaan, S.; Leinhos, M.; Aral, S.; Douglas, J.; Lipshutz, J. Springer-SBM; New York, NY: 2007.
   The ethics of public health practice for the prevention and control of sexually transmitted diseases;
   Behavioral Interventions for Prevention and Control of Sexually Transmitted Diseases; p. 517-548.
- Xu F, Sternberg M, Kottiri B, et al. Trends in herpes simplex virus type 1 and type 2 seroprevalence in the United States. JAMA. 2006; 296:964–973. [PubMed: 16926356]
- 11. Semaan, S.; Des Jarlais, D.; Malow, R.; Aral, S.; Douglas, J. Behavioral Interventions for Prevention and Control of Sexually Transmitted Diseases, Including HIV. Springer-SBM; New York, NY: 2007. Sexually transmitted diseases among illicit drug users in the United States: The need for interventions; p. 397-430.
- Des Jarlais DC, Friedman SR, Novick DM, et al. HIV-1 infection among intravenous drug users in Manhattan, New York City, from 1977 through 1987. JAMA. 1989; 261:1008–1012. [PubMed: 2915408]
- Des Jarlais D, Arasteh A, Hagan H, et al. Persistence and change in disparities in HIV infection among injecting drug users in New York City after large-scale syringe exchange. Am J Public Health. 2009; 99:S445–S451. [PubMed: 19797757]
- Des Jarlais D, Arasteh K, Perlis T, et al. Convergence of HIV seroprevalence among injecting and non-injecting drug users in New York City: A new stage in a very large HIV epidemic. AIDS. 2007; 21:231–235. [PubMed: 17197815]
- 15. Celum C, Wald A, Hughes J, et al. Effect of aciclovir on HIV-1 acquisition in herpes simplex virus 2 seropositive women and men who have sex with men: A randomised, double-blind, placebocontrolled trial. Lancet. 2008; 371:2109–2119. [PubMed: 18572080]
- 16. Watson-Jones D, Weiss H, Rusizoka M, et al. Effect of herpes simplex suppression on incidence of HIV among women in Tanzania. N Engl J Med. 2008; 358:1560–1571. [PubMed: 18337596]

17. Fisher J, Smith L. Secondary prevention of HIV infection: The current state of prevention for positives. Curr Opin HIV AIDS. 2009; 4:279–287. [PubMed: 19532065]



**Figure 1.** HIV and HSV2 prevalence by 10-year age groups among never-injecting drug users, NY, 2004–2007.



**Figure 2.**A, HIV and HSV2 infections by age among female never-injecting drug users, NY, 2004–2008. B, HIV and HSV2 infections by age among non-MSM male never-injecting drug users, NY, 2004–2008. C, HIV and HSV2 infections by age among MSM never-injecting drug users, NY, 2004–2008.

TABLE 1

Selected Demographic and Drug Use Characteristics of Never-Injecting Heroin and Cocaine Users, New York City, 2004–2009

	N (%)	
Total	1418 (100)	
Gender		
Males	1075 (76)	
Race/ethnicity		
Whites	74 (5)	
Blacks	951 (67)	
Hispanics	357 (25)	
Other/mixed	36 (3)	
MSM (% of males)	114 (11)	
Drug use		
Heroin	518 (37)	
Cocaine	586 (41)	
Crack cocaine	1055 (74)	
Average age (SD)*	42 (7)	
HIV+	233 (16)	
HSV-2+	859 (61)	

<sup>\*</sup>Average age and standard deviation of age in years.

TABLE 2

HSV-2 and HIV Prevalence by Demographic and Drug Use Characteristics Among Never-Injector Drug Users, New York City, 2004–2009

	Total N (%)	HSV-2+ N (%)	HIV+ N (%)
Total	1418 (100)	859 (61)	233 (16)
Gender/MSM			
Men (non-MSM)	956 (100)	482 (50)*	112 (12)*
MSM	114 (100)	82 (72)*	52 (46)*
Women	343 (100)	293 (85)*	69 (20)*
Race/ethnicity			
Whites	74 (100) 29 (39)*		$4(5)^{\dagger}$
Blacks	951 (100)	631 (66)*	171 $(18)^{\dagger}$
Hispanics	357 (100)	177 (50)*	$54 (15)^{\dagger}$
Other/mixed	36 (100)	22 (61)*	$4(11)^{\dagger}$
Age			
18–29	75 (100) 29 (39)		7 (9)
30–39	372 (100)	198 (53)‡	63 (17)
40–49	776 (100)	496 (64)‡	132 (17)
50+	193 (100)	136 (70) <sup>‡</sup>	31 (16)
Drug use			
Heroin	518 (100)	280 (54)*	51 (10)*
Cocaine	586 (100) 317 (54)*		69 (12)*
Crack cocaine	1055 (100)	055 (100) 668 (63)*	

Significant difference by  $\chi^2$  test.

Significant difference by Cochran-Armitage test for trend.

 $<sup>^*</sup>P < 0.001.$ 

 $<sup>^{\</sup>dagger}P < 0.05$ .

 $<sup>^{\</sup>ddagger}P < 0.001.$ 

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**TABLE 3**Recent Sexual Risk Behaviors by HSV-2 and HIV Status and Gender Among Never Injectors, New York City, 2004–2009

	No Infection N (%)	Only HSV-2 N (%)	Only HIV N (%)	Co-Infection N (%)
Men (non-MSM)	439 (100)	405 (100)	35 (100)	77 (100)
Sexually active	334 (76)	312 (77)	26 (76)	54 (70)
Multiple partners	156 (36)	159 (40)	13 (37)	25 (32)
Unprotected sex with				
Any partner*	260 (59)	235 (58)	15 (43)	26 (34)
Primary partner*	206 (47)	166 (41)	9 (26)	19 (25)
Casual partner	81 (18)	96 (24)	6 (17)	11 (14)
Client	8 (2)	10 (3)	0 (0)	0 (0)
Women	48 (100)	226 (100)	$2^{\dot{\mathcal{T}}}$	67 (100)
Sexually active	36 (77)	176 (79)	1	48 (72)
Multiple partners $^{\not \!$	9 (19)	79 (35)	1	13 (19)
Unprotected sex with				
Any partner	32 (67)	145 (64)	1	27 (40)
Primary partner <sup>§</sup>	27 (56)	120 (53)	0	21 (31)
Casual partner	5 (10)	12 (5)	0	2 (3)
Client	4 (8)	40 (18)	1	6 (9)

Significant difference by  $\chi^2$  test.

 $<sup>^*</sup>P < 0.001.$ 

 $<sup>^{\</sup>dagger}$ Percentages not calculated given small sample size of n = 2.

 $<sup>^{\</sup>ddagger}P < 0.05.$ 

 $<sup>^{\</sup>S}P < 0.01$ .