Decline in Herpes Simplex Virus Type 2 Among Non-Injecting Heroin and Cocaine Users in New York City, 2005 to 2014: Prospects for Avoiding a Resurgence of Human Immunodeficiency Virus

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Decline in HSV-2 among non-injecting heroin and cocaine users in New York City, 2005–14: Prospects for avoiding a resurgence of HIV

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Abstract

Background—Herpes simplex virus type II (HSV-2) infection increases both susceptibility to and transmissibility of HIV, and HSV-2 and HIV are often strongly associated in HIV epidemics. We assessed trends in HSV-2 prevalence among non-injecting drug users (NIDUs) when HIV prevalence declined from 16% to 8% among NIDUs in New York City.

Methods—Subjects were current non-injecting users of heroin and/or cocaine and who had never injected illicit drugs. 3157 NIDU subjects were recruited between 2005–2014 among persons entering Mount Sinai Beth Israel substance use treatment programs. Structured interviews, HIV and HSV-2 testing were administered. Change over time was assessed by comparing 2005–2010 to 2011–2014 time periods. HSV-2 incidence was estimated among persons who participated in multiple years.

Results—HSV-2 prevalence was strongly associated with HIV prevalence (OR=3.9, 95% CI 2.9–5.1) from 2005–2014. HSV-2 prevalence declined from 60% to 56% (p=0.01). The percentage of NIDUs with neither HSV-2 nor HIV infection increased from 37% to 43%, (p<0.001); the percentage with HSV-2/HIV co-infection declined from 13% to 6%, (p<0.001). Estimated HSV-2 incidence was 1 – 2/100 person-years at risk

Conclusions—There were parallel declines in HIV and HSV-2 among NIDUs in New York City from 2005 to 2014. The increase in the percentage of NIDUs with neither HSV-2 nor HIV infection, the decrease in the percentage with HSV-2/HIV co-infection, and the low to moderate

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Statement of Conflict of Interest

The funding agency had no role in the design, conduct, data analysis or report preparation for the study.

HSV-2 incidence suggest some population-level protection against resurgence of HIV. Prevention efforts should be strengthened to end the combined HIV/HSV-2 epidemic among NIDUs in the city.

Keywords

Non-injection drug use; HIV; Herpes Simplex 2; Crack cocaine; New York City

Introduction

Herpes simplex virus II (HSV-2) increases susceptibility to and transmissibility of HIV by a factor of two to three.[1] HSV-2 can create lesions that facilitate entry of HIV and also recruits target cells to genital epithelia which increase the likelihood of acquiring HIV. HSV-2 also increases the magnitude of HIV viremia in genital secretions of co-infected persons, facilitating transmission of HIV. HSV-2 has been a major driver of sexual transmission of HIV in sub-Saharan Africa[2] and among non-injecting drug users (NIDUs).[3] Population-attributable risk factors analyses suggest that HSV-2 infection accounts for approximately half of HIV infections and is a major factor in racial/ethnic disparities in HIV infection among NIDUs in New York City.[3]

We recently reported a significant decrease in HIV infection among NIDUs in New York City, from a prevalence of 16% in 2005–2010 to a prevalence of 8% in 2011–2014 ($p < 0.001$).[4] This included approximately 50% reductions in HIV among both persons who used intranasal heroin and who smoked crack cocaine. We also noted a very low HIV incidence among the NIDUs (0.12/100 person-years at risk (PYAR) (95% CI 0.003/100 – 0.65/100 PYAR)). In this report, we present data on the trend in HSV-2 prevalence in the same NIDU population in New York City during the same time period as the decrease in HIV prevalence, examine continuing associations between HIV and HSV-2 infection in this group and consider the possible implications for resurgence of HIV transmission in this high-risk group. We also consider the implications for heterosexual transmission of HIV among NIDUs in other areas of the US.

Materials and Methods

The data presented here were collected as part of a long-running research study of persons entering Mount Sinai Beth Israel drug detoxification and methadone maintenance programs in New York City. The methods for this “Risk Factors” study have been previously described,[5, 6] so only a summary will be presented here. The programs serve New York City as a whole and there were no changes in the requirements for entrance into the program over the study period.

For the analyses presented here, only persons who reported never having injected drugs are included. Hospital records and questionnaire results were checked for consistency regarding route of drug administration and subjects were examined for physical evidence of injecting.

In the detoxification program, 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 asked to participate in the study. As there was no relationship between the assignment of patients to wards and the order that the staff rotated through the wards, these procedures should produce an unbiased sample of persons entering the detoxification program. In the methadone program, newly admitted patients (those admitted in the previous month) were asked to participate in the research. Participants were paid $20 for their time and effort. In both programs, approximately 95% of those asked agreed to participate. Common reasons for non-participation included medical appointments or other scheduled activities that would not permit completion of study.

Written informed consent was obtained and a trained interviewer administered a computer-assisted structured questionnaire covering demographics, drug use, sexual risk behavior, and use of HIV prevention services. Most drug use and HIV risk behavior questions referred to the 6 months prior to the interview, prior to entry into the drug treatment programs. Participants were asked about multiple classes of drugs by different routes of administration.

Participants were seen by counselors for HIV pretest counseling and serum collection. HIV testing was conducted at the NYC Department of Health Laboratory using a commercial, enzyme-linked, immunosorbent assays (EIA) 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 conducted for all subjects beginning in 2005 and was performed by BioReference Laboratories using the Focus HerpeSelect 1 and 2 ELISA. The laboratory used an index value of 1.1 or greater for classifying a subject as HSV-2 seropositive and reported results as positive/negative for all assays. The HSV-2 reports also included index values for assays after 2006. As there is debate about the appropriate index value for seropositivity for the Focus,[7] we also examined the HSV-2 results using an index value of 3.0 for HSV-2 assays after 2006.

A major focus of this paper is to compare trends in HSV-2 among NIDUs to the recently reported decline in HIV prevalence among NIDUs[4] who were also recruited from the Mount Sinai Beth Israel drug treatment programs. We used a step-down trend test[8, 9] to identify the year when the change in HIV prevalence was significantly different from the overall fluctuations in HIV prevalence. This yielded two time periods; 2005–2010 and 2011–2014. In order to maintain parallel analysis between the previous HIV trends and the HSV-2 data reported here, we used the same total study period (2005–2014) and also compared the same two time periods—2005–2010 versus 2011–2014 to assess changes over time.

Subjects were permitted to participate on multiple occasions, though only once per calendar year. For trend analyses, we included persons who participated in different years in the data for each year, as these subject were part of the population of interest (persons entering Mount Sinai Beth Israel drug treatment programs in each year).

Subjects who were HSV-2 seronegative at their first study participation and then were HSV-2 seropositive at a later participation were used as the numerator for estimating HSV-2 incidence. The denominator was the total number of years between first and last participation for subjects who remained HSV-2 seronegative plus one half of the time

between the last seronegative participation and the first seropositive participation of the subjects who did seroconvert. (The time at risk for the seroconverters is based on an assumption that seroconversion occurred midway between last seronegative participation and first seropositive participation.) Confidence intervals for incidence values (95% CI) were calculated using the binomial test for calculating exact confidence intervals. Repeat participation subjects were matched on name, drug treatment program identification number, gender and date of birth to ensure that these were the same individuals participating on more than one occasion. We estimated HSV-2 incidence based on both the binary yes/no, 1.1 index value, and on a 3.0 index value.

We used Cuzick's test for trend, chi square tests and logistic regression for statistical testing. For logistic regression analyses, listwise deletion was used whenever data were missing, though there were relatively little missing data (< 3% for any variable).

Stata 12 software[10] was used for statistical analyses. The study was approved by the Mount Sinai Beth Israel Institutional Review Board.

Results

Table 1 presents the demographic characteristics, recent drug use, HIV and HSV-2 prevalence of the 3157 NIDUs recruited into the study between 2005 and 2014. The subjects were predominantly male (8% of the males reported male-with-male sexual intercourse in the 5 years prior to the interview), and African-American and/or Latino/a. The average age increased significantly between the two time periods, and there were modest changes in the male/female and racial/ethnic group distributions. Intranasal heroin use increased and smoking crack cocaine decreased (for the 6 months prior to interview) modestly. As noted in Methods, participants were asked about multiple types of drug use. Intranasal use of heroin and smoking crack cocaine were the two most frequently reported types of drug use. These two types of drug use were not mutually exclusive. There was considerable overlap among the heroin sniffers and crack smokers: for the combined 2005–2014 period 33% of crack smokers also reported intranasal heroin use and 48% of intranasal heroin users also reported smoking crack. HSV-2 and HIV prevalence both decreased; HSV-2 prevalence decreased from 60.2% in 2005–2010 to 55.6% in 2011–2014 while HIV prevalence decreased from 15.7% in 2005–2010 to 7.6% in 2011–2014. In part due to the overlap among crack smokers and intransal heroin users, there were parallel trends in HSV-2 prevalance among these two groups. (See Figure 1.) (Using an index value of 3.0 for determining HSV-2 seropositive status, HSV-2 prevalence was 55% in 2005–1010 and 51% in 2011–2014 (chi square = 4.2, $p < 0.05$.)

Factors associated with being HSV-2 seropositive

We used multivariable logistic regression with backwards elimination to examine whether the decline in HSV-2 prevalence between 2005–2010 and 2011–2014 remained significant when controlling for demographic characteristics and recent drug use. (These analyses used the 1.1 index value.) Results are presented in Table 2. The decline in HSV-2 prevalence remained statistically significant and the adjusted odds ratio (AOR = 0.82, 95% CI 0.70–

0.97, $p < 0.05$) was very similar to the unadjusted odds ratio for the decline in HSV-2 prevalence (OR = 0.83, 95% CI 0.72 – 0.96).

There was a significant increase of 4 years in the mean age of the NIDUs from 2005–2010 to 2011–2014 (see Table 1), and age was positively associated being HSV-2 seropositive (Table 2). Tables 3a and 3b presents HSV-2 prevalence by age category and the age structures of the 2005–2010 and 2011–2014 samples. There is a clear association of increasing HSV-2 prevalence with increasing age in each time period. There is also an indication of a cohort effect in the two samples. The cohort of persons aged 40 – 49 in 2005 –2010 and then aged 45 – 50+ in 2011–2014 constituted large percentages of the samples and had high HSV-2 seroprevalence in each time period.

Sexual Risk Behavior

Table 4 presents 2005–2010 versus 2011–2014 comparisons of sexual risk behaviors. There was a statistically significant reduction in the percentage of NIDUs who reported multiple sexual partners in the 6 months prior to the interview (chi square = 38.1, $p < 0.001$).

HIV and HSV-2 Infection

HSV-2 prevalence was strongly associated with HIV seroprevalence among the NIDUs during the total time period (OR = 3.9, 95% CI 2.9 – 5.1) and in both 2005–2010 (OR = 3.6, 95% CI 2.6 – 4.9) and 2011–2014 (OR = 4.5, 95% CI 2.6 – 8.0) time periods. These ORs were primarily a function of the high percentage of HIV seropositives who were also HSV-2 seropositive. In 2005–2010, 82% of HIV seropositives were also HSV-2 seropositive; in the 2011–2014, 84% of HIV seropositives were also HSV-2 seropositive.

We examined changes in the distribution of HSV-2 and HIV among the NIDUs—the percentages of subjects with 1) neither HSV-2 nor HIV infection, 2) HSV-2 infection only, 3) HIV infection only, and 4) HSV-2/HIV co-infection over the 2005–2014 period. These are graphed in Figure 2. The percentage of NIDUs with neither HSV-2 nor HIV infection increased from 37% in 2005–2010 to 43% in 2011–2014, (chi square = 11.6, $p = 0.001$). The percentage with HSV-2/HIV co-infections significantly decreased from 13% in 2005–2010 to 6% of the 2011–2014, chi square = 33.4, $p < 0.001$. The percentage with HIV mono-infection also decreased from 2.8% to 1.2%, chi square =8.6, $p < 0.01$, though this percentage was quite low throughout the entire 2005–2014 period. The percentage with HSV-2 mono-infection did not change significantly (from 47% to 49%).

HSV-2/HIV co-infected NIDUs on ART

A high percentage of our HSV-2/HIV co-infected NIDUs were on ART, 75% in 2005–2010 and 85% in 2011–2014. (Though this increase was not statistically significant, $p = 0.11$)

HSV-2 Incidence

As noted in the Methods section, we examined possible HSV-2 seroconversion, using the laboratory positive/negative reports for 2005–2014 and using an index value of 3.0 for 2007–2014. Using the laboratory positive/negative reports (which were based on an index value of 1.1), there were 10 seroconversions in 447 person-years at risk, for an incidence rate of

2.2/100 PY, 95% CI 0.12 to 4.1/100PY. Using an index value of 3.0 gave 4 seroconversions in 494 person-years, for an incidence rate of 0.8/100 PY, 95% CI 0.2 to 2.1/100 PY. Note the substantial overlap in the 95% CIs; we would suggest 1– 2/100 PY as a "best estimate" of HSV-2 incidence over the 2005–2014 period. The incidence rates were slightly lower in 2011–2014 than in 2005–2010, but there were not sufficient numbers of HSV-2 seroconversions for meaningful statistical analysis of factors associated with seroconversion.

Discussion

As both HIV and HSV-2 viruses produce chronic infections with persistent antibodies, HIV or HSV-2 seroprevalence will decline in an at-risk population only through turnover in the population—when the sum of seropositive persons leaving the population plus the number of new seronegative persons entering the population is greater than the sum of seronegative persons leaving the population plus the seroconverters.

The data on the HSV-2 incidence rate and the decline in HSV-2 prevalence over time permit some estimation of turnover in this NIDU population. We observed an HSV-2 incidence of 1 –2/100 PY and there was a 4.5 year time difference between the midpoint of the 2005–2010 time period and the 2011–2014 time period. In the absence of turnover in the population, we would have expected the HSV-2 prevalence to rise to between 64% and 68% (initial prevalence of 60% plus (1–2/100 PY incidence x 10 years x 40% of HSV-2 who were initially seronegative)). Thus, turnover in the population led to a reduction of approximately 8% to 12% from the expected HSV-2 prevalence, and was generating a reduction in prevalence of approximately 1% per year over the 2005–2014 period.

The relatively modest number of younger NIDUs in 2011–2014 (see Tables 3a and 3b) suggest that the primary factor in population turnover was the loss of HSV-2 seropositives rather than entry of HSV-2 seronegatives into the NIDU population. There are many reasons why HIV/HSV-2 co-infected NIDUs might leave the population of active non-injecting drug users, including disability, death, cessation of non-injecting heroin and/or cocaine use, transition to injection drug use, overdose, or factors related to aging.

The declines in HIV and HSV-2 among NIDUs occurred in the context of large-scale prevention programs in New York City. New York has implemented several evidence-based programs that would potentially reduce HIV and HSV-2 transmission among NIDUs/crack cocaine users, including the NYC condom distribution program (begun in 2007),[11] a policy of providing ART to all HIV seropositives (adopted in 2011),[12] and providing detoxification services for NIDUs/crack cocaine users. New York City also has a large methadone maintenance treatment system, which would be appropriate for many of the intranasal heroin users. As a substantial percentage of the crack cocaine users also used heroin, it is possible that methadone maintenance may be helpful for some of them in reducing HSV-2/HIV risk. The condom distribution program is quite large with over 30 million free condoms distributed per year. The provision of ART to HIV seropositive NIDUs has a high coverage, as noted in the ART data above. (We would also note that providing multiple interventions on a public health scale and permitting individuals to select which interventions to utilize is likely to produce the greatest reductions in HIV/HSV-2 transmission.)

The decline in HSV-2 prevalence was modest, certainly too modest to account for the substantial reduction in HIV prevalence (from 16% to 8% we observed in the same NIDU population over the same time period). The trends in HSV-2 that we observed from 2005 to 2014, however, do suggest some population-level protection against a resurgence of HIV among the NIDUs. First, there was a decline in the potential HIV transmission from HSV-2/HIV co-infected persons. The percentage of NIDUs with HSV-2/HIV co-infection in the NIDU population decreased substantially, so that there would be fewer NIDUs in whom HSV-2 infection might facilitate HIV transmission. There was also a large percentage of the HSV-2/HIV co-infected NIDUs (85% during the second period) who were on ART, which would also reduce infectiousness.

Second, the percentage of NIDUs without either HSV-2 or HIV infection increased. These NIDUs would not be subject to HSV-2 facilitating acquisition of HIV.

Third, the significant reduction in the percentage of NIDUs reporting multiple sexual partners in the 6 months prior to the interview should also contribute to reductions in HIV and HSV-2 transmission, as having multiple sexual partners within short periods of time increases the likelihood of transmission for a wide variety of sexually transmitted diseases.[13–15] Continuation of these trends should reduce the chances of resurgence of HIV among NIDUs in the New York City.

While the above trends are clearly in a positive direction, the problem of HSV-2 facilitated transmission of HIV among NIDUs remains a substantial public health issue. HSV-2 prevalence remains high in the NIDU population and it is higher in socially disadvantaged groups—MSM, females, African-Americans, both in New York City (see Tables 1 and 2) and nationally in the US. HSV-2 among persons who use drugs has particularly been a problem in large urban areas in the US[16] and it may also be emerging as a problem among rural drug users.[17] HSV-2 suppressive therapy has not reduced HIV transmission in large clinical trials.[18] We do not have an effective medication for the treatment of stimulant drug (cocaine, amphetamine type stimulants) disorders. And there is the emergence of novel psychoactive substances (NPS) which may lead to increases in drug use-related unsafe sexual behavior. Thus it is important that the large HIV prevention programs for NIDUs in New York City be maintained and strengthened if feasible.

Limitations

Several limitations of this study should be mentioned. First, all of the subjects were voluntarily entering treatment for drug problems, considerable caution should be exercised in generalizing to non-injecting drug users who use at levels that do not lead them to seek treatment for their drug use. However, previous comparisons of HIV among persons enter Mount Sinai Beth Israel drug treatment programs with persons recruited from the community (and from other drug treatment programs) show great consistency across the various recruitment sites.[19]

Second, the research design is serial cross-sectional surveys, so that we do not have direct data on the numbers of persons who left the active non-injecting drug use population. Third,

our estimation of HSV-2 (and HIV) incidence comes from persons who repeatedly entered treatment for their non-injecting drug use. These NIDUs would presumably be at higher risk for drug-use facilitated transmission of HIV and HSV-2, so that our observed HSV-2 incidence may be a high estimate. Fourth, we had only a modest percentage (8% of males) who reported male-with-male sexual activity and very few subjects who reported methamphetamine use, so that our results should not be generalized to MSM or to methamphetamine users in general. Fifth, we do not have data on sero-concordance/discordance or rate of partner change in the primary and casual sexual partnerships of our participants. Changes in these partnerships could serve as mechanisms for decreased transmission of HIV and HSV-2. Finally, there is no surveillance system specific to HIV or HSV-2 among non-injecting users of heroin and/or cocaine, so that we cannot match the trends in our sample with surveillance data.

We doubt that these limitations would have generated the patterns observed in the data reported here or in our previous report of declining HIV prevalence among NIDUs in New York City.[20] Rather, we believe that these patterns were observed despite the limitations of the study.

Generalization to other areas

Current HIV surveillance systems do not include non-injecting drug use as a factor influencing transmission risk and do not include HSV-2 infection among persons diagnosed with HIV. Thus we have limited long-term data on the extent to which non-injecting drug use and HSV-2 infection combine to facilitate HIV transmission. The national decline in HSV-2 prevalence in NHANES[21] and the decline in new HIV diagnoses attributable to heterosexual transmission[22] are certainly positive trends and are consistent with the data in this report.

Semaan and colleagues reviewed US studies of HSV-2 and HIV among persons who use drugs (PWUD, both injecting and non-injecting drug use)[23] and concluded that “HSV-2 seroprevalence is high among PWUD, necessitating research on development and implementation of science-based public health interventions for HSV-2 infection and HSV-2/HIV co-infections.” While the data reported here do show clear improvement in the HSV-2/HIV situation among NIDUs in New York City, we believe that the Semaan et al. conclusion still holds for NIDUs in New York City and in the country as a whole. We would add to the Semaan at all conclusion that evidence-based interventions should be implemented on a public health scale and should be maintained over long periods of time.

Conclusions

New York City experienced a combined high seroprevalence epidemic of HIV and HSV-2 infection among NIDUs. Over the last decade there has been a substantial reduction in HIV prevalence and a modest decline in HSV-2 prevalence. These have occurred in the context of large-scale safer sex/condom social marketing and relatively high coverage of ART for HIV seropositive NIDUs. HSV-2 incidence is low to moderate, and the patterns in the reduced HSV-2 prevalence suggest some population level protection against resurgence of HIV transmission, but the potential for HSV-2 to facilitate HIV transmission remains as a

substantial public health issue, particularly among females, MSM and African-American NIDUs. Maintenance and strengthening prevention programs should have the potential for "ending"[3] the dual HSV-2/HIV epidemic among NIDUs in New York City.

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References

1. Barnabas RV, Celum C. Infectious co-factors in HIV-1 transmission herpes simplex virus type-2 and HIV-1: new insights and interventions. Curr HIV Res. 2012; 10(3):228–37. [PubMed: 22384842]
2. Rajagopal, S.; Magaret, A.; Mugo, N.; Wald, A. Open forum infectious diseases. Oxford University Press; 2014. Incidence of herpes simplex virus type 2 infections in Africa: a systematic review; p. ofu043
3. Des Jarlais DC, Arasteh K, McKnight C, et al. HSV-2 Co-infection as a driver of HIV transmission among heterosexual non-injecting drug users in New York City. PloS one. 2014; 9(1)
4. Des Jarlais D, McKnight CM, Arasteh K, Feelemyer J, Perlman DC, Hagan H, Russell E, Cooper H. A perfect storm: crack cocaine, HSV-2 and HIV among non-injecting drug users in New York City. Sub Use Misuse. 2013
5. 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; 261:1008–12. [PubMed: 2915408]
6. Des Jarlais D, Arasteh A, Hagan H, McKnight C, Perlman D, Friedman S. 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(Suppl 2):S445–S51. [PubMed: 19797757]
7. De Baetselier I, Menten J, Cuylaerts V, et al. Prevalence and incidence estimation of HSV-2 by two IgG ELISA methods among South African women at high risk of HIV. PloS one. 2015; 10(3):e0120207. [PubMed: 25799522]
8. Organisation for Economic Co-operation and Development. Current Approaches in the Statistical Analysis of Ecotoxicity Data: A guidance to application. Paris: 2014. OECD Series on Testing and Assessment
9. Lin D, Shkedy Z, Yekutieli D, et al. Testing for trends in dose-response microarray experiments: a comparison of several testing procedures, multiplicity and resampling-based inference. Stat Appl Genet Mol Biol. 2007; 6(1)
10. Stata 12 [computer program]. College Station, Texas: 2012.
11. Burke RC, Wilson J, Bernstein KT, et al. The NYC Condom: use and acceptability of New York City's branded condom. Am J Public Health. 2009; 99(12):2178–80. [PubMed: 19834001]
12. Farley, T. Health Department Releases New HIV Treatment Recommendations. 2011.
13. Adimora AA, Schoenbach VJ. Social context, sexual networks, and racial disparities in rates of sexually transmitted infections. J Infect Dis. 2005; 191(Supplement 1):S115–S22. [PubMed: 15627221]
14. Liljeros F, Edling CR, Amaral LAN. Sexual networks: implications for the transmission of sexually transmitted infections. Microbes Infect. 2003; 5(2):189–96. [PubMed: 12650777]
15. Rosenberg MD, Gurvey JE, Adler N, Dunlop MB, Ellen JM. Concurrent sex partners and risk for sexually transmitted diseases among adolescents. Sex Transm Dis. 1999; 26(4):208–12. [PubMed: 10225587]
16. Oster AM, Sternberg M, Nebenzahl S, et al. Prevalence of HIV, sexually transmitted infections, and viral hepatitis by urbanicity, among men who have sex with men, injection drug users, and heterosexuals in the United States. Sex Transm Dis. 2014; 41(4):272–9. [PubMed: 24622641]

17. Stephens DB, Young AM, Mullins UL, Havens JR. Correlates to seroprevalent herpes simplex virus type 2 among rural Appalachian drug users. J Med Virol. 2016; 88(3):512–20. [PubMed: 26288383]

18. 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, placebo-controlled trial. Lancet. 2008; 371:2109–19. [PubMed: 18572080]

19. Des Jarlais DC, Arasteh K, McKnight C, et al. Consistent Estimates of Very Low HIV Incidence Among People Who Inject Drugs: New York City, 2005–2014. Am J Public Health. 2016; 106(3): 503–8. [PubMed: 26794160]

20. Des Jarlais DC, McKnight C, Arasteh K, et al. A Perfect Storm: Crack Cocaine, HSV-2, and HIV Among Non-Injecting Drug Users in New York City. Subst Use Misuse. 2014; 49(7):783–92. [PubMed: 24502371]

21. Xu F, Sternberg MR, Kottiri BJ, et al. Trends in herpes simplex virus type 1 and type 2 seroprevalence in the United States. JAMA. 2006; 296(8):964–73. [PubMed: 16926356]

22. Johnson AS, Hall HI, Hu X, Lansky A, Holtgrave DR, Mermin J. Trends in diagnoses of HIV infection in the United States, 2002–2011. JAMA. 2014; 312(4):432–4. [PubMed: 25038362]

23. Semaan S, Leinhos M, Neumann MS. Public health strategies for prevention and control of HSV-2 in persons who use drugs in the United States. Drug Alcohol Depend. 2013; 131(3):182–97. [PubMed: 23647730]

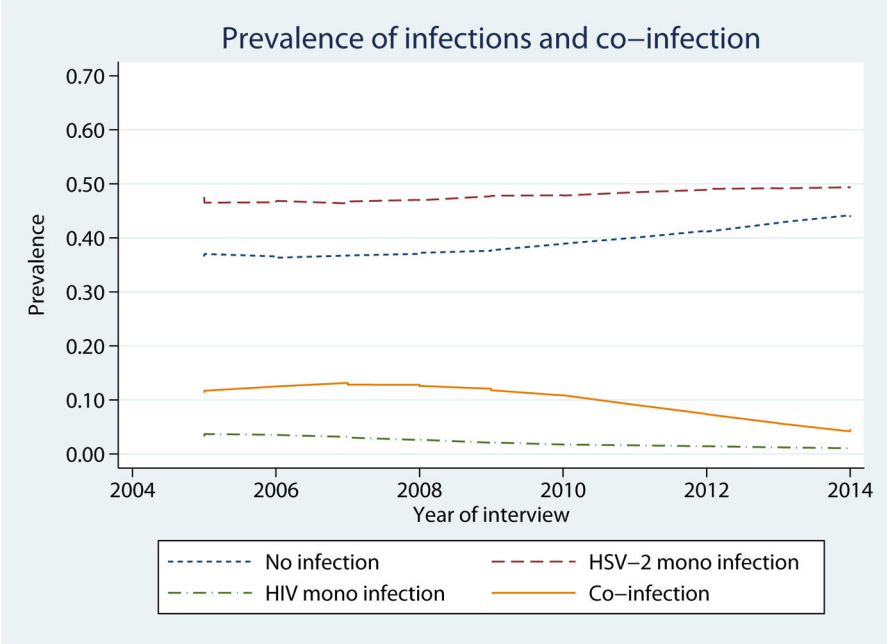

Figure 1.
Trends in HSV-2 Prevalence among heroin and crack cocaine NIDU, 2004–2014

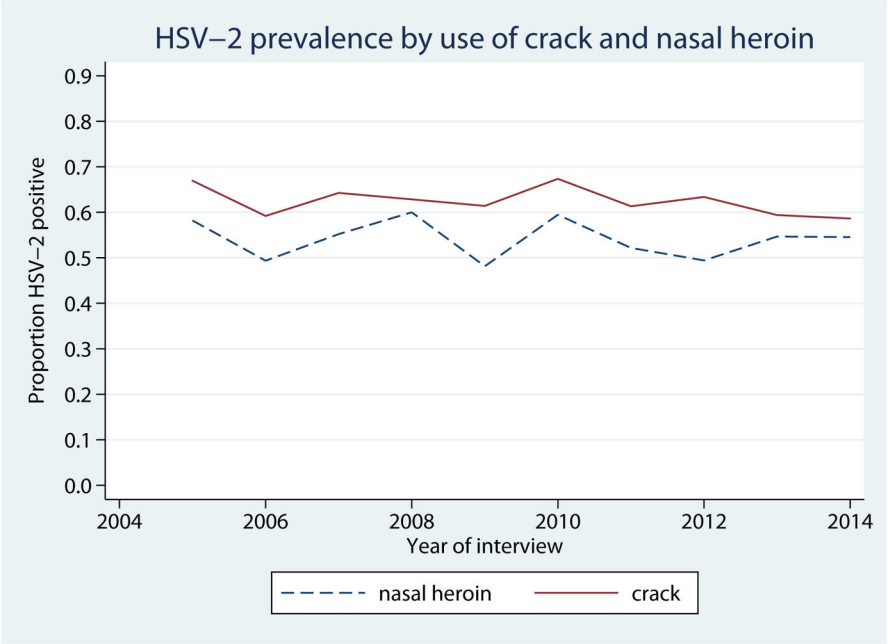

Figure 2.
Trends in HIV and HSV-2 Prevalence among NIDUs, 2004–2014

Table 1

Demographics, drug use characteristics, HIV and HSV-2 prevalence of NIDUs in New York City 2005–2014

	Time Period					
	2005–2010		**2011–2014**		**2005–2014**	
Average age (SD) *	42 (7.5)		46 (8.6)		44 (8.2)	
	N	%	N	%	N	%
Gender *						
Male	1468	76.7	1022	82.2	2490	78.9
Female	440	23.0	220	17.7	660	20.9
Race/ethnicity *						
White	104	5.4	91	7.3	195	6.2
African American	1283	67.1	784	63.0	2067	65.5
Latino/a	475	24.8	344	27.7	819	25.9
Heroin/intranasal *	724	37.8	757	61.1	1481	47.0
Speedball/intranasal	161	8.4	118	9.5	279	8.8
Cocaine/ intranasal	782	40.9	549	44.1	1331	42.2
Crack Cocaine/smoked *	1409	73.7	741	59.6	2150	68.1
HIV+ *	296	15.7	93	7.6	389	12.5
HSV-2+ *	1152	60.2	692	55.6	1844	58.4

* significant difference ($p<0.05$) across time periods by t-test (age) and chi-square test (all other variables)

Table 2

Multivariable logistic model of HSV-2 prevalence among NIDUs in New York City 2005–2014

	2005–2014
	AOR (95% CI)
Time period	
2005–2010	1 (ref)
2011–2014	0.82 (0.70–0.97)
Gender/MSM	
Non-MSM Male	1 (ref)
MSM	2.38 (1.72–3.30)
Female	7.22 (5.61–9.29)
Race ethnicity	
White	1 (ref)
African American	3.83 (2.68–5.47)
Latino/a	2.39 (1.65–3.46)
Age (continuous variable by year)	1.04 (1.03–1.06)
Drug use	
Cocaine/intranasal	0.86 (0.74–1.01)
Crack cocaine/smoked	1.21 (1.02–1.44)

Table 3a

HSV-2 prevalence by age groups among NIDUs in New York City 2005–2014

	2005–2010			2011–2014		
	HSV-2+			HSV-2+		
Age group	**Total N**	**N**	**%**	**Total N**	**N**	**%**
18–24	35	11	31.4	20	3	15.0
25–29	77	29	37.7	41	11	26.8
30–34	148	76	51.4	75	35	46.7
35–39	326	177	54.3	96	49	51.0
40–44	551	344	62.4	235	127	54.0
45–49	499	325	65.1	339	207	61.1
50+	276	190	68.8	438	260	59.4

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Table 3b

Age groups by time-periods among NIDUs in New York City 2005–2014

	Time Period			
	2005–2010		2011–2014	
Age group	**N**	**%**	**N**	**%**
18–24	35	1.8	20	1.6
25–29	77	4.0	41	3.3
30–34	148	7.7	75	6.0
35–39	326	17.1	96	7.7
40–44	551	28.8	235	18.9
45–49	499	26.1	339	27.3
50+	276	14.4	438	35.2

Table 4

Unsafe sex with primary and casual partners and having multiple sex partners among NIDUs in New York City 2005–2014

	Time Period				
	2005–2010		2011–2014		P
	N	%	N	%	
Total	1913	100	1244	100	
Unsafe sex w/ primary partner	782	40.8	526	42.3	0.5
Unsafe sex w/ casual partner	332	17.4	195	15.7	0.2
Multiple sex partners *	686	35.9	316	25.4	<0.0001

* significant difference ($p<0.05$) across time periods by chi-square test