

Reductions in hepatitis C virus and HIV infections among injecting drug users in New York City, 1990–2001

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Objective: To assess trends in HIV, hepatitis C virus (HCV) and HIV/HCV infection among injecting drug users (IDU) from 1990 to 2001 in New York City. The 1990–2001 time period included a very large expansion of syringe exchange in New York City, from 250 000 to 3 000 000 syringes exchanged annually.

Methods: Cross-sectional seroprevalence surveys of IDU entering drug abuse treatment in New York City, with sample sizes for HCV of 72 in 1990–1991 and 412 in 2000–2001. A structured risk behavior questionnaire was administered, and HIV and HCV testing were conducted. HCV testing was performed on de-linked stored serum samples.

Results: Over the 1990–2001 period, HIV prevalence declined from 54 to 13%. HCV prevalence declined from 80 to 59% among HIV-seronegative individuals, and from 90 to 63% overall. The estimated HCV incidence in 2000–2001 among new injectors was 18 per 100 person-years at risk.

Conclusions: The large-scale expansion of syringe exchange was temporally associated with large reductions in both HIV and HCV prevalence. The prevalence and incidence of HCV, however, still remain at high levels among IDU in New York City.

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Introduction

Both HIV and hepatitis C virus (HCV) are extremely important blood-borne pathogens for injecting drug users (IDU). Historically, HIV infection has been almost uniformly fatal, although the development of highly active antiretroviral therapy may make HIV infection a manageable chronic disease. For HCV, approximately 80% of those infected develop chronic infection, and approximately 25% of chronic infections lead to serious complications, including cirrhosis and liver cancer [1,2].

Both HIV and HCV are transmitted parenterally, and there have been suggestions that HCV infection should be used as an outcome measure for evaluating HIV prevention programmes [3]. Whether current HIV prevention programmes will have a major effect on HCV transmission, however, is still an open question.

A number of studies have found a high prevalence of HCV in areas where HIV prevalence has been kept low (under 10%). For example, HCV prevalence is 82% in IDU in Seattle, USA [4], 70% in IDU in Melbourne,

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Australia [5], and 80% in IDU in Geneva, Switzerland [6]. Some studies have shown substantial HCV incidence in the presence of low HIV incidence (1/100 person-years or less). This has been observed in Melbourne IDU, in whom HCV incidence has been reported to be between 15 and 40/100 person-years [5], in Seattle IDU with an annual HCV incidence of 21/100 person-years versus 0.2/100 person-years for HIV [4], and 25/100 person-years HCV incidence in San Francisco IDU [7].

There may be several factors that make reducing HCV transmission more difficult than reducing HIV transmission. In most areas there are many more IDU capable of transmitting HCV than are capable of transmitting HIV. Second, HCV is more efficiently transmitted than HIV [8], and may be transmitted through sharing drug preparation equipment (cottons, cookers, rinse water) much more efficiently than HIV [9,10]. Third, HCV may not raise as much concern and generate as much behavior change among IDU as does HIV [11]. In combination with a substantial local variation in access to sterile injection equipment, these factors may lead to great variations in the risk of HCV transmission [12,13].

Despite these rather discouraging results, there are some indications that HIV prevention programmes may at least be slowing the rates of HCV transmission among IDU. Before the year 2000, estimates of HCV prevalence in IDU reported in the literature ranged between 65 and 95% [14]. However, more recent studies have reported an HCV seroprevalence in IDU below 50% [15,16], and there have been a number of recent studies that have reported HCV prevalence among new injectors at levels lower than older studies (although still high in absolute terms) [17–21].

We report here on trends in HCV infection and HIV/HCV co-infection among IDU in New York City from 1990 to 2001. The 1990–2001 time period included a very large expansion of syringe exchange in New York City, from 250 000 to 3 000 000 syringes exchanged annually. This expansion of syringe exchange was temporally associated with a large reduction in HIV prevalence among IDU in New York City [22]. The HIV data will also be reviewed here for comparison.

Methods

Subject recruitment

The data reported here are part of an ongoing series of studies of IDU entering the Beth Israel Medical Center drug detoxification programme in New York City (methods previously described in [23–27]). The detoxification programme serves the city as a whole; approximately half of its patients live in Manhattan, one quarter in Brooklyn, one fifth in the Bronx, and the rest (5%) elsewhere. The programme is quite

large, with 5000–7000 admissions per year. The criteria for admission to the programme are: (i) being 18 years of age or older; and (ii) being sufficiently dependent upon a psychoactive drug that inpatient detoxification is indicated. There were no substantive changes in programme admission criteria or study recruitment procedures over the 1990–2002 time period.

Patients in the detoxification programme were selected to produce an unbiased sample of IDU in the programme. Research staff visited the general admission wards of the programme in a pre-set order and examined the intake records to identify patients admitted within the past 3 days who had reported injecting illicit drugs within the previous 2 months. All of these newly admitted IDU in the specific ward were then asked to participate in the study. The study was fully described to each potential subject, and a signed informed consent was obtained from those who agreed to participate. Some eligible patients were not able to participate because of appointments scheduled by hospital staff (for X-rays, appointments with social workers, physicians, etc.). Among patients approached by our interviewers, willingness to participate was over 95%. After all of the patients admitted to a specific ward in the 3-day period had been asked to participate, the interviewer moved to the next ward in the pre-set order. Data collection was continuous throughout the study period.

A structured questionnaire covering demographics, drug use, injection, sexual risk behavior, and the use of HIV prevention services was administered by a trained interviewer. Risk behaviors were assessed for the 6 months before the interview. After completion of the interview, the participant was referred to an HIV counselor for pre-test counseling and HIV testing. A separate informed consent was obtained for HIV testing. Leftover serum was aliquotted and stored at -70°C .

Hepatitis C virus testing

HCV testing was not part of the original study protocol, but was performed on stored sera after the removal of identifiers (de-linking). We tested a random sample of stored sera from 48 IDU enrolled in the study from 1990 to 1991 and a random sample of stored sera from 349 HIV-seronegative IDU enrolled in the study from 2000 to 2001. The relatively small sample from 1990 to 1991 was selected with the expectation that HCV prevalence among our IDU subjects would be very high during this period and because of the need to conserve sera from the earlier years of the study. The larger sample size for 2000–2001 was selected so that we might examine HCV prevalence among various groups of IDU, including among different racial/ethnic groups and among new injectors.

We were also able to perform HCV testing on an additional 20% random sample of the HIV-positive

subjects in the study for whom we performed the serologic testing algorithm for recent HIV seroconversions (STARHS) testing [28]. This gave an additional sample of 21 HIV-seropositive individuals from 1990 to 1991 and an additional sample of 34 HIV-seropositive individuals from 2000 to 2001 (none of these were duplicates of the randomly drawn samples from 1990 to 1991 or 2000 to 2001).

As the STARHS testing was performed only on confirmed HIV-seropositive individuals, the addition of these samples creates an overrepresentation of HIV-seropositive individuals in both 1990–1991 and 2000–2001. We thus present the data for HCV infection among HIV-seronegative subjects and HIV-seropositive subjects separately, and then use weighted averaging to generate estimates of total HCV prevalence and HIV/HCV co-infection for each time period.

In order to conserve sera, we did not use the last aliquot for any randomly selected subject. The selection procedure was thus not fully random, but comparisons of the subject characteristics of selected versus not selected subjects did not show any differences with respect to age, sex or race/ethnicity (data not presented, available from the first author).

Samples were tested for HCV antibodies with the Abbott HCV enzyme immunoassay (EIA) 2.0 (Abbott Laboratories, Abbott Park, IL, USA). Test results showing a signal to cut-off ratio of 1.0 or greater were said to be reactive and were considered to represent hepatitis C infection for purposes of this study. Confirmatory testing using recombinant immunoblot assay was not performed, but 91% of the reactive samples were positive for HCV antibodies based on an EIA signal to cut-off ratio of more than 3.5 and were thus very likely to be anti-HCV positive. This antibody testing would not detect individuals who were recently infected and had not yet developed detectable levels of anti-HCV.

We used chi-squared tests and Fisher's exact tests to compare HCV prevalence between the two time periods.

The study was approved by the institutional review boards (human subject protection/ethical review) of the Beth Israel Medical Center, the National Development and Research Institutes, and the New York State Department of Health.

Results

Table 1 shows the demographic characteristics of the HIV-negative and HIV-positive subjects tested for HCV (recruited in 1990–1991 and in 2000–2001). Given the purposive sampling among the HIV-negative subjects, we

Table 1. Demographic characteristics of HIV-negative and HIV-positive injecting drug users tested for anti-hepatitis C virus.

	N (%) HIV negative	N (%) HIV positive
Race/ethnicity		
White	105 (29)	17 (15)
Black	62 (17)	39 (34)
Hispanic	192 (53)	59 (51)
Sex		
Male	293 (80)	97 (84)
Female	72 (20)	18 (16)
Average age (SD)	35 (8.2)	39 (6.9)

did not perform formal statistical comparisons of these two groups. In our full analyses of HIV prevalence, however, African-American subjects were substantially more likely to be HIV seropositive than white subjects in each year over the entire 1990–2001 time period [22], and this is reflected in the higher percentage of African-Americans in the HIV-positive group. In addition, HIV-positive subjects tend to be older, reflecting more time at risk while injecting drugs.

Table 2 shows HCV seroprevalence among the HIV-negative subjects, the HIV-positive subjects, weighted average HCV prevalence and the prevalence of HIV/HCV co-infection (also based on weighted averages) for 1990–1991 and 2000–2001. There are substantial reductions in HCV prevalence from 1990–1991 to 2000–2001.

As HCV is generally much easier to transmit than HIV through sharing of drug injection equipment, subjects who are HIV seropositive and HCV seronegative are of some interest. As shown in Table 2, there were no subjects who were HIV positive and HCV negative in 1990–1991 and 13 out of 71 (18%) who were HIV seropositive and HCV seronegative in 2000–2001. We compared demographic characteristics (age, sex, race/ethnicity) and drug injection variables (primary drug injected, frequency of injection in the past 6 months, new versus long-term injectors) of these 13 with the 58 subjects who were both HIV and HCV seropositive in 2000–2001. The only significant difference ($P < 0.005$) was that four out of 13 of the HIV-seropositive/HCV-seronegative individuals were new injectors (injecting for 6 years or less) versus only two out of 58 subjects (< 4%) who were seropositive for both HIV and HCV.

Drug users are very likely to be HCV seronegative when they start injecting drugs, so that HCV prevalence among new injectors can be used as a measure of recent infections in this group. Table 3 shows HCV prevalence among HIV-seronegative new injectors (individuals injecting for 6 years or less) among the subjects from 1990 to 1991 and 2000 to 2001 (the 6-year cut-off was selected in order to have a reasonable number of 'new injectors' in each time period). Even with the modest sample size of

Table 2. Prevalence of hepatitis C virus among injecting drug users in New York City (1990–1991 and 2000–2001).

	1990–1991	2000–2001
Prevalence of HCV/total HIV-negative IDU ^a		
No. of HCV positives/no. of HIV negatives	20/25	200/340
Percentage (with 95% confidence limits)	80% (59%, 93%)	59% (53%, 64%)
Prevalence of HCV/total HIV positive IDU ^b		
No. of HCV positives/no. of HIV positives	44/44	58/71
Percentage (with 95% confidence limits)	100%	82% (71%, 90%)
Prevalence of HCV among all detox IDU, using weighted frequencies (with 95% confidence limits)	91% (83%, 98%)	62% (58%, 67%)
Co-prevalence of HIV/HCV among all detox IDU, using weighted frequencies (with 95% confidence limits)	53% (40%, 65%)	13% (9%, 16%)

HCV, Hepatitis C virus; IDU, injecting drug users.

^aChi-square = 4.36, $P = 0.034$.

^bFisher's exact $P = 0.0016$.

new injectors for 1990–1991, there was a statistically significant difference in HCV prevalence among new injectors. (We had very modest numbers of HIV-seropositive new injectors, 19 for 1990–1991 and only 10 for 2001–2001, so that weighted averaging is questionable. As expected, however, the weighted averages for the new injectors also show a substantial difference in HCV prevalence, 86% in 1990–1991 versus 38% in 2000–2001.)

Assuming that all new injectors were HCV negative when they began injecting drugs, and those who were HCV seropositive were infected at the midpoint between starting to inject drugs and the time of data collection, there would be a total of 50 HCV infections and 275 person-years at risk among the new injectors in 2000–2001, giving an estimated HCV incidence of 18/100 person-years at risk (95% confidence interval 14 to 23/100-person years).

As noted above, we have found consistent racial/ethnic differences in HIV seroprevalence among our subjects over the 1990–2001 time period, with prevalence highest among African-American subjects, intermediate for Hispanic subjects and lowest for white subjects in each year [22]. Table 4 shows HIV prevalence among all of our subjects in 1990–1991 and 2000–2001 (previously

Table 3. Prevalence of hepatitis C virus among HIV-negative new injectors in New York City (1990–1991 and 2000–2001).

Period	No. HCV positives/total no. Percentage (with 95% confidence limits)
1990–1991	8/10 80% (44%, 98%)
2000–2001	48/127 38% (29%, 47%)

Fisher's exact $P = 0.015$.

Table 4. Prevalence of HIV and hepatitis C virus by race/ethnicity among injecting drug users in New York City (1990–1991 and 2000–2001).

Period	Race/ethnicity	No. (%) seropositive
HIV Prevalence 1990–1991	White	33 (32)
	Black	101 (61)
	Hispanic	135 (56)
2000–2001	White	17 (9)
	Black	46 (29)
	Hispanic	50 (14)
HCV prevalence 2000–2001	White	72 (65)
	Black	45 (59)
	Hispanic	139 (63)

reported in Des Jarlais *et al.* [22]) and HCV seroprevalence among the subjects from 2000 to 2001 who were tested for HCV. HCV prevalence was very similar among the three major racial/ethnic groups.

Discussion

Before considering the implications of these data, two limitations of the study should be considered. First, IDU entering the Beth Israel detoxification programme are clearly not a random sample of IDU in New York City. However, the decline in HIV prevalence seen among the detoxification patients is parallel to declines in HIV prevalence seen among IDU recruited from other treatment sites and among street-recruited IDU during the mid to late 1990s [29]. Given that HIV was declining in many studies of IDU in New York over this time period, it would appear likely that the decline in HCV observed in this study was also occurring in other groups of IDU in the city.

Second, we did not conduct confirmatory testing of the HCV-positive individuals. However, the specificity of the HCV EIA assay is greater than 99% [30]. In this study, we had a total of 312 HCV-seropositive individuals, and would thus expect two to three false positives. This small number of false positives clearly would not affect the pattern of lower HCV prevalence in 2000–2001 compared with 1990–1991 (see Table 2).

Third, the expansion of syringe exchange in New York City must be considered a 'natural experiment' and not a randomized clinical trial. Syringe exchange was legalized and greatly expanded in New York City beginning in late 1992. Before this legalization and expansion, there were approximately 250 000 syringes exchanged per year. By 2000–2001, approximately 3 000 000 syringes were exchanged per year [22]. This was associated with large declines in HIV prevalence (data shown above) and in HIV incidence (from 3/100 person-years at risk to 1/100 person-years at risk as well as the decline in HCV prevalence) [28]. However, drawing causal inferences from temporal associations must always be carried out with care, and other HIV prevention services for IDU, including community outreach programmes, voluntary HIV counseling and testing, drug abuse treatment, and treatment for HIV infection were also available during this period. For a detailed discussion of the temporal relationships between the expansion of the syringe exchange programmes and the declines in HIV prevalence and incidence, see Des Jarlais *et al.* [28].

The data presented here also show a substantial reduction in HCV prevalence among IDU entering detoxification treatment in New York City over the 1990–1991 to 2000–2001 time period. As individuals co-infected with HIV and HCV are at high risk of morbidity and mortality from both infections, a loss of dually infected individuals in the active IDU population is almost certainly an important factor in the overall reductions in HIV and HCV prevalence. The estimated HCV prevalence of 38% and the incidence of 18/100 person-years among the new injectors in 2000–2001 show that new injectors are becoming infected at a substantial rate in New York, and that there are still opportunities for preventing HCV infection among new injectors (see also Hagan *et al.* [17]).

Even with these favorable trends, HCV infection is still a major problem among IDU in New York City. The 62% seroprevalence level in 2000–2001 cannot be considered acceptable from a public health perspective. There have been recent increases in efforts to reduce HCV among IDU in the city, with syringe exchange programmes, drug abuse treatment programmes and community outreach programmes putting greater emphasis on HCV education and prevention. This has included warnings against sharing drug preparation equipment (cottons, cookers, rinse water), which may transmit HCV, and the increased availability of counseling and testing for HCV. Some

efforts are also being made to provide treatment for HCV to drug users. The long-term effectiveness of the various efforts to reduce HCV infection among IDU in New York City remains to be determined. The current situation also presents opportunities to work with new injectors before they are infected, either to help them stop injecting or to practise extremely hygienic safer injection.

The differences by race/ethnicity in HIV and HCV deserve comment. As noted above, there are persistent differences in HIV prevalence rates, with rates highest among African-American IDU, intermediate among Hispanic IDU, and lowest among white IDU. In contrast, the HCV prevalence rates do not differ by race/ethnicity. As HCV is transmitted predominantly through multi-person use of drug injection equipment (including preparation equipment), one is led to the belief that injection risks are roughly equivalent among these three racial/ethnic groups. As HIV is transmitted both through the sharing of injection equipment and unprotected sexual activities, the differences in HIV prevalence may primarily be a function of differences in unsafe sexual behaviors. The recent injectors who are HIV seropositive but HCV seronegative also suggest an increasing importance of the sexual transmission of HIV.

There have been important declines in HIV infection, HCV infection and HIV/HCV co-infection among IDU in New York City over the past decade, and there are now increased efforts to prevent HCV infection. The extent to which these declines continue over the next decade should be monitored closely.

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