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Risk of Hepatitis C Virus Infection among Young Adult Injection Drug Users Who Share Injection Equipment

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Designing studies to examine hepatitis C virus (HCV) transmission via the shared use of drug injection paraphernalia *other than syringes* is difficult because of saturation levels of HCV infection in most samples of injection drug users (IDUs). The authors measured the incidence of HCV infection in a large cohort of young IDUs from Chicago, Illinois, and determined the risk of HCV seroconversion associated with specific forms of sharing injection paraphernalia. From 1997 to 1999, serum samples obtained from 702 IDUs aged 18–30 years were screened for HCV antibodies; prevalence was 27%. Seronegative participants were tested for HCV antibodies at baseline, at 6 months, and at 12 months. During 290 person-years of follow-up, 29 participants seroconverted (incidence: 10.0/100 person-years). The adjusted relative hazard of seroconversion, controlling for demographic and drug-use covariates, was highest for sharing "cookers" (relative hazard = 4.1, 95% confidence interval: 1.4, 11.8), followed by sharing cotton filters (relative hazard = 2.4, 95% confidence interval: 1.1, 5.0). Risks associated with syringe-sharing and sharing of rinse water were elevated but not significant. After adjustment for syringe-sharing, sharing cookers remained the strongest predictor of seroconversion (relative hazard = 3.5, 95% confidence interval: 1.3, 9.9). The authors conclude that sharing of injection equipment other than syringes may be an important cause of HCV transmission between IDUs. *Am J Epidemiol* 2002;155:645–53.

equipment contamination; hepatitis C; hepatitis C-like viruses; incidence; needle-exchange programs; needle sharing; risk-taking; substance abuse, intravenous

In the United States, injection drug users (IDUs) are the group at highest risk for infection with hepatitis C virus (HCV) (1). Estimates suggest that more than 60 percent of new cases of HCV infection are associated with injection drug use (2), and numerous studies have found prevalence levels of 70–90 percent among long-term IDUs (3–7). Two characteristics of HCV have been hypothesized to contribute to saturation levels of infection in IDU populations. First, parenteral transmission of the virus appears to be extremely efficient. By comparing incidence rates among occupationally exposed populations, researchers have estimated that parenteral transmission of HCV is 10-fold more efficient than that of human immunodeficiency virus (HIV) (8, 9). Second, HCV has a stronger tendency towards chronicity than other forms of viral hepatitis. Approximately 85 percent of persons acutely infected with HCV develop persistent viremia; this generates a large reservoir of infected IDUs with potential for spreading the virus through parenteral contact (10–12).

In the past decade, IDUs have responded to the acquired immunodeficiency syndrome epidemic by reducing the extent to which they share syringes (13–20), but most studies show continued high levels of sharing of other injection paraphernalia (21–23). These include "cookers" (containers used to mix and heat drugs), cotton filters, and rinse water. In most injection sessions, drugs are placed in a cooker and dissolved in water. The solution is then drawn into a syringe through a cotton filter to strain out "impurities." Researchers have termed the multiperson use of these types of equipment "indirect sharing" to differentiate this from the direct use of shared syringes (24). The high efficiency of parenteral HCV transmission has led to concern that infection occurs through indirect sharing (6). Attempting to determine the transmission risk associated with sharing of different kinds of injection paraphernalia is difficult, because no reliable

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Abbreviations: CI, confidence interval; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IDU(s), injection drug user(s).

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tissue culture system exists for HCV (25). It is also difficult to design prospective epidemiologic studies of uninfected IDUs with sufficient person-years at risk, seroconversion events, and statistical power to accurately isolate the independent effects of sharing practices other than sharing of syringes.

The following study was undertaken to examine the associations between different injection-related risk practices and transmission of HCV. To accomplish this, we examined street-recruited young adult IDUs, a population with moderate levels of infection prevalence, and we assembled a cohort large enough to use prospective survival analysis methods.

MATERIALS AND METHODS

Study population

Between August 1997 and April 1999, young adult IDUs aged 18–30 years were recruited from the greater Chicago, Illinois, region and enrolled in a prospective study. The cohort was developed as part of the Collaborative Injection Drug Users Study II, a multisite longitudinal study conducted under a cooperative agreement with the Centers for Disease Control and Prevention. Participants were monitored at enrollment and at two follow-up visits made 6 months apart. The study was conducted from storefront offices in four low-income Chicago neighborhoods, each selected for its high concentration of drug users and its distinct racial and ethnic composition. Persons were enrolled in the study if they had proof of an eligible birthdate and reported having injected drugs in the past 6 months. Recent injection drug use was verified by inspecting for stigmata, such as scars or abscesses. When stigmata were absent, we interviewed enrollees to ascertain their familiarity with injection routines. Study protocols were explained to participants, and informed consent was obtained prior to data collection. At the close of the interview, staff members counseled participants about the risks of HIV and viral hepatitis associated with sharing syringes and other paraphernalia, as well as risks associated with unsafe sex practices. All participants were given information about drug treatment programs, on-site hepatitis B vaccination, and other available services. The study was approved by institutional review boards at the Centers for Disease Control and Prevention and the University of Illinois at Chicago. All participants were compensated ($25 for the baseline interview, $30 for the 6-month follow-up interview, and $35 for the 12-month follow-up interview).

Participants were recruited through street outreach, targeted advertising, and peer referrals. Street recruiting by former IDUs was done in areas such as youth hangouts, "shooting galleries" (places where drug users gather to inject drugs and perhaps be assisted in injecting), and illicit drug markets. Advertisements were placed in alternative magazines, in newspapers, and on college campuses. In a version of respondent-driven sampling (26), each newly interviewed participant received three coupons to distribute to eligible peers. When a peer redeemed one of these numbered coupons by enrolling in the study, the peer recruiter received an incentive fee of $10.

This analysis included all participants who were susceptible to hepatitis C infection (negative for antibodies to HCV) at the initial visit. All susceptible participants were followed up so they could be examined for seroconversion, the main outcome measure. Seroconversion was defined as the presence of antibodies to HCV in a previously seronegative participant. The cutoff date for follow-up of participants was September 30, 1999.

Data collection and laboratory methods

Blood specimens were collected for HCV antibody screening. Serum samples were stored locally at –20°C, and approximately once per month they were batch-shipped overnight on dry ice to the Centers for Disease Control and Prevention's hepatitis laboratory for testing. Samples were tested for antibodies to HCV using a second-generation antibody enzyme-linked immunosorbent assay (Abbott HCV enzyme immunoassay 2.0; Abbott Laboratories, Chicago, Illinois). All positive samples were retested twice by enzyme-linked immunosorbent assay, but no confirmatory testing was performed on baseline positive samples because of the high positive predictive value of repeat reactive enzyme immunoassay testing in this population when samples are tested against a confirmatory assay (100 percent in a sample of 100 specimens from this multicenter study and >95 percent in a previous, similar study (27)). All identified seroconversions were confirmed using a supplemental recombinant immunoblot assay (recombinant immunoblot assay 3.0; Chiron Corporation, Emeryville, California), and a final qualitative polymerase chain reaction test (Roche Amplicor, Branchburg, New Jersey) was employed for persons with indeterminate recombinant immunoblot assay results.

Trained interviewers administered a standardized face-to-face interview in a private room. The survey instrument was developed by the Centers for Disease Control and Prevention and the principal investigators from each study site. Respondents were asked about sociodemographic characteristics, drug use during the past 6 months, and recent sexual behaviors.

Variables

Self-reported injection-related risk behaviors in the past 6 months were assessed at enrollment. Risk factors for seroconversion in this analysis, coded dichotomously as yes/no, included having engaged in any of the following behaviors in the previous 6 months: 1) receptive syringe-sharing, 2) "backloading," a street term for injecting with a syringe filled with drugs that were first mixed or measured in someone else's syringe, 3) sharing of cookers, 4) sharing of cotton filters, and 5) sharing of rinse water. "Sharing" was defined as using the item in question along with other people or after other people had used it.

Baseline measures examined as covariates included age, gender, race/ethnicity, educational level, homelessness during the past 6 months, place of residence (urban or suburban Chicago), duration of injection, frequency of injection dur-

ing the past 6 months (daily or less), types of other drugs used in the past 6 months (specifically, crack use and cocaine injecting), and any use of needle-exchange programs in the past 6 months. Injection settings were considered dichotomously, including visiting a shooting gallery (ever vs. never) and injecting most often at home or in a car during the past 6 months (yes/no). Variables designed to measure the extent of social interactions involving injecting behavior were also dichotomized as yes/no, identifying participants who had always injected with other people during the past 6 months, those with a sex partner who injected drugs, and those who reported ever initiating others into injecting. Sex risk variables included engaging in commercial sex and number of sex partners (in quartiles) in the past 6 months.

Statistical methods

Incidence rates were calculated using person-time methods (28). To calculate incidence, we defined date of infection acquisition as the midpoint between the last seronegative test and the first seropositive test. Survival time was determined as the time from baseline to HCV seroconversion (the event of interest), death, or the study cutoff date, whichever came first. Because the exact date of seroconversion was not known, estimated cumulative probabilities for time to seroconversion were generated for different injection-related risk groups using Turnbull's method, which produces estimates appropriate for interval-censored data (29). Interval-censored Cox proportional hazards models were generated to obtain unadjusted and adjusted relative hazard estimates and associated 95 percent confidence intervals for covariates of interest (30). If the addition of any covariate demonstrated a confounding influence on the injection-risk parameter estimates or if it was a significant independent predictor itself, it was retained in the final set of models. We also tested for interaction between injection-risk exposure variables and other covariates included in the final models and retained any terms showing statistical significance ($\alpha = 0.05$). Finally, we tested the proportional hazards assumption in each model using methods appropriate for data with a known time to event, since methods of testing proportional hazards assumptions are not widely available for interval-censored data.

Final multivariate models were constructed with fixed measures of risk behavior taken from baseline survey data. Because we were specifically interested in the independent effects of each of the "indirect" sharing practices, we completed a hierarchy of models. Having performed multivariate analyses separately for each of the risk practices, we then built three models that also included syringe-sharing as a covariate to examine the estimated independent effects of sharing of cookers, cotton, and rinse water on time to HCV seroconversion.

RESULTS

Baseline findings

The study population consisted of 702 active, young adult IDUs with available hepatitis C antibody test results. Mean age at baseline was 24 years (median, 23), and 65 percent of the participants were male. Most participants (58 percent) were White; 22 percent were Latino, and 17 percent were African-American. Nearly 40 percent of the participants reported a suburban zip code for the address where they had lived or slept most often during the past 6 months. Most of the participants were relatively new initiates to drug injection: Half had begun injecting during the 2 years prior to enrollment (mean = 3 years; range, <1–20 years). In this sample, the proportion of participants who reported having shared injection paraphernalia in the previous 6 months was high: 50 percent had shared syringes, 62 percent had shared cookers, 45 percent had shared cotton, 54 percent had shared rinse water, and 20 percent had engaged in backloading. Overall, almost three quarters (74 percent) of the participants reported having shared injection paraphernalia of any type (cotton, cookers, water, or syringes) during the past 6 months. At enrollment, 192 participants tested positive for hepatitis C (a prevalence of 27 percent), and 510 (73 percent) were hepatitis C-seronegative. Factors associated with HCV seropositivity in the total sample have been described elsewhere (31).

Follow-up analysis

Of the 510 HCV-seronegative IDUs enrolled in the study, seven (1 percent) died, and 374 (74 percent) completed at least one follow-up survey. Of the participants with follow-up information, 94 percent ($n = 353$) provided sera for an HCV antibody test. The 21 participants for whom we had no sera or insufficient sera were excluded from this analysis, which gave us an effective follow-up rate of 69 percent (353/510). Participants retained in the analysis were retested for HCV seroconversion. The median duration of follow-up was 330 days (standard deviation 120.6). Most participants had a follow-up time of less than 15 months (75th percentile = 399 days), but five participants were interviewed after being released from prison, and their follow-up times were somewhat extended, ranging between 608 days and 724 days. During a total of 290.0 observed person-years of risk in this study, we documented 29 cases of incident HCV infection, for a crude incidence rate of 10.0 per 100 person-years (95 percent confidence interval (CI): 6.7, 14.4).

There were few differences between IDUs retained in the study and those who failed to return (table 1). In univariate analysis, factors associated with loss to follow-up included male gender (odds ratio = 1.8, 95 percent CI: 1.2, 2.8), race/ethnicity other than Black (odds ratio = 1.9, 95 percent CI: 1.1, 3.5), injection of cocaine during the past 6 months (odds ratio = 2.2, 95 percent CI: 1.5, 3.3), and not having a sex partner who injected drugs (odds ratio = 1.5, 95 percent CI: 1.0, 2.2). No significant associations were observed between injection-related risk practices at baseline and retention in the study. In a multivariate logistic model predicting loss to follow-up, two of the four variables remained statistically significant: male gender (odds ratio = 1.7, 95 percent CI: 1.1, 2.6) and injecting cocaine (odds ratio = 2.3, 95 percent CI: 1.5, 3.7).

TABLE 1. Characteristics of injection drug users who were seronegative for antibodies to hepatitic C virus at enrollment and follow-up, Chicago, Illinois, 1997–1999

Characteristic	Baseline (n = 510)		Follow-up			
			6 months (n = 353)		12 months (n = 189)	
	No.	%	No.	%	No.	%
Age (years)						
18–22	270	52.9	184	52.1	89	47.1
23–26	128	25.1	86	24.4	45	23.8
27–30	112	22.0	83	23.5	55	29.1
Race/ethnicity						
White	335	65.7	226	64.0	105	55.6
Black	90	17.7	66	12.9	36	19.1
Latino	85	16.7	60	11.8	48	25.4
Gender						
Male	343	67.3	225	63.7	114	60.3
Female	167	32.8	128	36.3	75	39.7
Homeless in the past 6 months	136	26.7	96	27.2	45	23.8
Suburban residence	230	45.1	153	43.3	68	36.0
Duration of drug injecting (years)						
<1	183	35.9	130	36.8	69	36.5
1–<3	183	35.9	123	34.8	62	32.8
3–<5	81	15.9	53	15.0	29	15.3
≥5	63	12.4	47	13.3	29	15.3
Frequency of injection (once/day or more often)	204	40.0	141	39.9	57	30.2
Cocaine or speedball* injection in the past 6 months	164	32.2	97	27.5	34	18.0
Sharing syringes in the past 6 months	251	49.2	168	47.6	46	24.3
Sharing a cooker/cotton filter/rinse water in the past 6 months	353	69.2	199	56.4	84	44.4
Having a sex partner who injected drugs	281	55.1	203	57.5	113	60.0
Recruited by coupon method	297	58.2	199	57.3	104	55.0

* Cocaine mixed with heroin or amphetamine.

Risk factors for HCV seroconversion

In univariate analyses (table 2), we found no significant association between risk of HCV seroconversion and age, gender, race, place of residence, homelessness, or education. Although results were not significant, relative hazards were slightly elevated for younger, less educated, and Latino participants. Few drug-use practices were associated with an elevated risk of seroconversion. Daily injectors, who accounted for 40 percent of the sample, were more than two times as likely as those who injected less frequently to become infected with HCV. We found no significant associations between types of places where IDUs injected most often and their risk of becoming infected with HCV. Similarly, the extent to which participants reported injecting with other IDUs did not predict seroconversion, nor did their use of needle-exchange programs. Sexual risk practices, such as engaging in commercial sex (relative hazard = 1.5, 95 percent CI: 0.7, 3.3) and having four or more sex partners in the past 6 months (75th percentile vs. none: relative hazard = 1.1, 95 percent CI: 0.3, 3.8), were not associated with risk of HCV seroconversion.

Cumulative probabilities of seroconversion at both 6 months and 12 months were elevated for persons sharing paraphernalia in comparison with those not sharing (table 3). The disparity in cumulative probabilities was greatest between persons who shared cookers and those who did not, and the unadjusted relative hazard for sharing cookers was significantly elevated. While risks were elevated for sharing of syringes, cotton, and rinse water and for backloading, they were statistically nonsignificant.

After including all factors shown to exert a confounding influence, plus factors associated with HCV seroconversion in univariate analyses, in each of our models examining a particular sharing practice, we found that the magnitude of risk associated with time to HCV seroconversion for each of

TABLE 2. Unadjusted estimated relative hazard of hepatitis C virus seroconversion by exposure group among 353 susceptible young adult injection drug users, Chicago, Illinois, 1997–1999

	Total no.	%	No. of seroconversions	Relative hazard	95% confidence interval
Demographic covariates					
Age (years)					
18–22	184	52	18	1	
23–26	86	24	3	0.34	0.10, 1.17
27–30	83	24	8	0.83	0.36, 1.92
Female gender	128	36	11	1.00	0.47, 2.09
Race					
White	226	64	17	1	
Latino	60	17	8	1.51	0.63, 3.61
Black	67	19	4	0.71	0.26, 2.00
Residence					
Urban	200	57	19	1	
Suburban	153	43	10	0.82	0.20, 3.32
Homeless in the past 6 months	96	27	7	0.76	0.31, 1.86
Education					
High school not completed	132	37	15	1	
High school diploma	122	35	10	0.65	0.29, 1.49
Some higher education	99	28	4	0.44	0.16, 1.20
Drug-use practices					
Duration of drug injecting (years)					
<1	130	37	10	1	
1–<3	123	35	11	1.11	0.47, 2.60
3–<5	53	15	7	1.72	0.65, 4.56
≥5	47	13	1	0.25	0.03, 2.01
Injection frequency					
Less than daily	212	60	13	1	
Daily or more often	141	40	16	2.11	1.02, 4.35
Cocaine injection in the past 6 months	97	28	5	0.53	0.20, 1.39
Any crack use in the past 6 months	227	65	21	1.33	0.74, 2.38
Ever injecting in a shooting gallery	79	23	6	0.89	0.36, 2.18
Injected most often at home in the past 6 months	153	43	12	0.93	0.44, 1.98
Use of a needle-exchange program in the past 6 months	110	31	10	1.29	0.60, 2.79
Ever initiating others into drug injecting	116	33	7	0.70	0.30, 1.63
Always injecting in groups	104	30	10	1.26	0.58, 2.70
Having a sex partner who injected drugs	203	58	15	0.92	0.45, 1.88

the sharing practices increased. Sharing of cookers and sharing of cotton filters were both statistically significant predictors of HCV transmission (table 4), whereas receptive syringe-sharing, sharing of rinse water, and backloading were not. In each model, the covariate of daily injection showed a robust positive association with seroconversion, and education was protective.

The main purpose of our analysis was to examine and isolate the independent effects of sharing paraphernalia *other than syringes*; therefore, we added the measurement of receptive syringe-sharing into each of the models examining cookers, cotton, and water (table 5). When we did so, sharing cookers and sharing rinse water were independent predictors of seroconversion, whereas the effect of sharing cotton was no longer statistically significant. Daily injection also continued to be an independent predictor of time to seroconversion. Standard errors in this final model did not inflate greatly, which suggests that collinearity between these risk practices was moderate.

In our study, few participants (7 percent) reported not injecting drugs during the follow-up period. Additional analyses (data not shown) excluding participants who ceased injecting showed that the addition or exclusion of persons who did not inject during follow-up did not alter the associations between sharing practices and seroconversion risk.

DISCUSSION

This study provides epidemiologic evidence that sharing of drug injection paraphernalia other than syringes may cause transmission of HCV among IDUs. In particular, the positive association between HCV seroconversion and sharing of cookers, the most commonly reported risk practice in this group, appears to be more robust than associations found with other sharing behaviors, including the sharing of syringes. In our study, it was not possible to discern exactly why some indirect sharing practices had a stronger associa-

TABLE 3. Cumulative probability of hepatitis C virus seroconversion by length of time exposed and unadjusted relative hazard estimates, by type of injection-related risk practice, among 353 susceptible young adult injection drug users, Chicago, Illinois, 1997–1999

Injection-related equipment-sharing practice	Cumulative probability		Relative hazard	95% confidence interval
	At 6 months (n = 353)	At 12 months (n = 189)		
Receptively sharing syringes				
No	3.6	7.7	1	
Yes	6.4	13.2	1.82	0.86, 3.86
Sharing cookers				
No	1.9	1.9	1	
Yes	6.0	13.9	3.13	1.20, 8.16
Sharing cotton filters				
No	4.8	5.9	1	
Yes	5.4	14.2	1.88	0.91, 3.90
Sharing rinse water				
No	4.4	4.4	1	
Yes	5.1	13.0	1.99	0.91, 4.36
Backloading*				
No	4.4	9.9	1	
Yes	5.4	12.4	1.29	0.55, 3.01

* Injecting with a syringe filled with drugs that were first mixed or measured in someone else's syringe.

TABLE 4. Adjusted relative hazard of time to hepatitis C virus seroconversion among 353 susceptible young adult injection drug users, Chicago, Illinois, 1997–1999

Injection-related risk exposure*	Adjusted relative hazard†	95% confidence interval
Receptively sharing syringes	2.10	0.90, 4.90
Sharing cookers	4.07	1.41, 11.78
Sharing cotton filters	2.38	1.14, 4.98
Sharing rinse water	2.68	0.86, 8.35
Backloading‡	1.38	0.58, 3.31

* Self-report of engaging in the behavior in the past 6 months (any vs. none).

† Adjusted for education, homelessness, place of residence, frequency of injection, and cocaine injection.

‡ Injecting with a syringe filled with drugs that were first mixed or measured in someone else's syringe.

tion with HCV transmission than syringe-sharing. However, prevention messages regarding the risks associated with syringe-sharing have been disseminated for a longer time and have circulated more widely (32–36) than messages regarding the risks of sharing cookers, cotton, and rinse water (6, 21, 37, 38). Surveys and ethnographic data likewise indicate that a far greater proportion of IDUs are unaware of the potential risks associated with sharing paraphernalia other than syringes compared with the risk of sharing syringes (21, 37). The historical focus on preventing syringe-sharing, while undoubtedly effective at reducing the transmission of bloodborne pathogens among IDUs, may have influenced how IDUs share syringes without greatly affecting their indirect sharing practices. IDUs may be restricting the pool of persons with whom they share a syringe to those they know well or trust, and it is possible that they are less discriminating in their indirect sharing practices. If so, a potentially less efficient mode of HCV transmission than syringe-sharing, such as sharing of cookers, may currently be responsible for many new infections among young adult IDUs.

This study lacked the precision to ascertain whether or not sharing of cookers transmits HCV more readily than sharing of other injection paraphernalia. Confidence intervals around the risk estimates overlapped for the different types of paraphernalia, and there is a possibility that the magnitudes of the different risk estimates were similar. However, several factors suggest that the practice of sharing cookers may provide substantial transmission opportunities. Our study and others have found that cookers are shared among IDUs more often than other equipment (21, 24). Ethnographic studies that have followed IDUs through repeated sessions of drug injecting have also indicated that IDUs tend to retain and reuse cookers longer than either cotton filters or rinse water (39). Therefore, opportunities for contaminating cookers with HCV are perhaps greater than those for contaminating either cotton or rinse water.

While a definitive causal link has yet to be established between indirect sharing practices and HIV or HCV transmission, two laboratory studies have confirmed the presence and viability of HIV in cotton, cookers, and rinse water (39, 40). Both studies strongly suggested that transmission of HIV is possible by sharing such equipment. Evidence suggests that HCV is more efficiently transmitted through low-dose percutaneous exposure (e.g., a contaminated needle-stick) than is HIV, which raises the question of whether sharing cookers, cotton, or water would be more efficient at transmitting HCV

TABLE 5. Final adjusted results from relative hazard models designed to isolate the independent effects of sharing of different types of drug-injection equipment (adjusted for syringe-sharing) on time to hepatitis C virus seroconversion among 353 susceptible young adult injection drug users, Chicago, Illinois, 1997–1999

	Multivariate models controlling for syringe-sharing behavior					
	Model 1		Model 2		Model 3	
	Adjusted RH*	95% CI*	Adjusted RH	95% CI	Adjusted RH	95% CI
Injection-related risk exposures						
Sharing cookers	3.54	1.26, 9.94				
Sharing cotton filters			1.98	0.88, 4.46		
Sharing rinse water					2.29	1.01, 5.20
Sharing syringes	1.40	0.67, 2.94	1.61	0.68, 3.80	1.62	0.75, 3.50
Demographic covariates						
High school diploma	0.55	0.26, 1.16	0.49	0.23, 1.06	0.46	0.22, 0.97
Homeless in the past 6 months	0.63	0.25, 1.58	0.62	0.25, 1.58	0.62	0.25, 1.55
Suburban residence	0.62	0.29, 1.34	0.62	0.29, 1.36	0.56	0.25, 1.25
Drug-use covariates						
Daily injection in the past 6 months	2.31	1.11, 4.82	2.37	1.12, 5.00	2.18	1.06, 4.51
Cocaine injection in the past 6 months	0.50	0.18, 1.36	0.47	0.17, 1.32	0.48	0.17, 1.35

* RH, relative hazard; CI, confidence interval.

than HIV. Studies are needed to determine the presence and viability of HCV in these environments. Since no reliable tissue culture system exists for HCV, nonlaboratory transmission viability studies are needed. Animal transmission studies might prove useful, but the only effective animal model for HCV is the chimpanzee, which would make such studies costly (41). Findings from epidemiologic studies are thus likely to remain important in clarifying HCV transmission routes and risk practices until better viability studies can be conducted.

To date, four longitudinal studies have addressed HCV incidence and risk factors for HCV seroconversion among IDUs in the United States (6, 42–44). Three of the studies (6, 42, 44) suggested that sharing of injection paraphernalia other than syringes may be responsible for some proportion of new infections, but this association was formally studied in only two (42, 44). In Baltimore, Maryland, researchers showed the shared use of cookers to be a significant predictor of HCV seroconversion in comparison with referent groups of persons who ceased injecting altogether (42). More recently, in a study conducted in Seattle, Washington, investigators demonstrated that sharing of cotton and cookers, examined together, was an important and statistically significant risk factor for HCV seroconversion among a subgroup of active IDUs (44). The behaviors were not examined separately because of lack of statistical power. Both of these studies identified HCV-seronegative persons from parent samples that were largely composed of long-term injectors, where HCV prevalence had already reached at least 85 percent.

Our study contributes to this growing body of research in several ways. First, the study explicitly examined independent associations between the shared use of each type of injection paraphernalia and HCV seroconversion. Second, the recruitment of young IDUs, who often had been recently initiated into injection drug use and therefore had had limited exposure to HCV, made it possible to identify a large pool of uninfected individuals and to use powerful analytical techniques. Third, young IDUs probably constitute the largest group in the United States currently at high risk for HCV infection, and research on this population is scant. Therefore, our findings have strong relevance to current prevention efforts to reduce HCV infection.

One of our findings was that frequency of injecting was an independent predictor of seroconversion. While duration of injecting is often highly associated with HCV seroprevalence in cross-sectional studies (4, 5, 43–46), the frequency with which someone injects, measured during a limited period of time, is perhaps the broadest indicator of potential exposure to contaminated injection equipment in prospective studies.

This study had several limitations. First, the study population was a convenience sample of young IDUs in Chicago, and the true size and characteristics of this population remain unknown. Although we used multiple recruiting sites and methods to reduce sampling biases, the sample was not randomly selected. The extent to which our findings can be generalized to other young IDUs is therefore unknown. Systematic differences in recruitment techniques by risk group could have introduced selection biases into the study, but we found that method of recruitment was not associated with time to seroconversion, loss to follow-up, or injection equipment risk practices at enrollment (data not shown).

Second, although we attained a follow-up rate of 74 percent, we were unable to obtain full longitudinal information on all of our participants, and differential loss to follow-up may have biased the study findings. When comparing persons who returned for a follow-up visit and those who did not, we observed no differences with respect to injection-related risk practices, duration or frequency of injection,

age, race/ethnicity, place of residence, or homelessness. Disparities were observed only with respect to gender and cocaine injecting in the previous 6 months. Only the latter characteristic, cocaine injecting, appeared influential with regard to risk of seroconversion. However, when we reexamined the final model without adjusting for cocaine injection, we found little difference in the observed association between sharing of cookers and time to seroconversion (data not shown); this suggests that the influence of cocaine injecting on this association was minimal.

Third, exposure and covariate behaviors in this study were based on self-reported data. It is possible that participants may have been systematically less likely to report sharing of syringes than sharing of other equipment because of the greater stigma or perceived risk attached to sharing of syringes. However, the lack of statistical significance observed with syringe-sharing was also observed with the sharing of rinse water and cotton filters in different models. This suggests that any underreporting of syringe-sharing might not have systematically biased its association with seroconversion.

Exposures were also assessed prior to the observation period, and this analysis did not take interim or follow-up behaviors into account. In our early analyses, using survival methods that assumed seroconversion to occur at the midpoint between two interviews, we incorporated time-dependent sharing-behavior data from the two follow-up periods (data not shown). While findings were comparable to those using fixed preobservation exposures, we could not confirm that exposures preceded seroconversions during follow-up. We therefore chose to develop our subsequent interval-censored analyses using only the fixed exposures, ensuring an appropriate time sequence between exposure and disease.

Our final limitation relates to the lack of statistical power in this study to detect small associations, particularly when assessing transmission associated with different yet related sharing practices. While the large number of young adult IDUs enrolled in this study allowed us to conduct standard multivariate survival analyses to examine risks associated with time to HCV seroconversion, the short follow-up period and the limited number of events resulted in our study's having insufficient power to detect small relative hazards.

In this study, we identified relatively high rates of new HCV infection among susceptible young adult IDUs, and our findings indicate that IDUs who share paraphernalia other than syringes are at increased risk for HCV seroconversion. Among IDUs, current awareness of these transmission risks is low. Prevention messages and campaigns should be revised to alert active IDUs to the importance of reducing or eliminating *all* equipment-sharing practices. Other strategies designed to minimize the need to share paraphernalia should also be developed, including the proactive distribution of cookers and cotton filters in needle-exchange programs. Accessible HCV infection counseling and testing services should also be made available. Until the transmission risks of sharing all injection equipment, not just syringes, are more widely recognized, rapid HCV transmission may continue to occur among IDUs.

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