Reduced Risk of Hepatitis B and Hepatitis C among Injection Drug Users in the Tacoma Syringe Exchange Program

ABSTRACT

Objectives. This case–control study examined the association between syringe exchange use and hepatitis B and C in injection drug users.

Methods. Case patients included 28 injection drug users with acute hepatitis B and 20 with acute hepatitis C reported to the health department in a sentinel hepatitis surveillance county; control subjects were injection drug users with no markers of exposure to hepatitis B or C (n = 38 and 26, respectively) attending health department services during the same period. Data were abstracted from clinic records.

Results. Seventy-five percent of case patients with hepatitis B and 26% of control subjects had never used the exchange; similar proportions were found for the hepatitis C case and control groups. After adjustment for demographic characteristics and duration of injecting drugs, nonuse of the exchange was associated with a sixfold greater risk of hepatitis B (odds ratio [OR] = 5.5; 95% confidence interval [CI] = 1.5, 20.4) and a sevenfold greater risk of hepatitis C (OR = 7.3; 95% CI = 1.6, 32.8).

Conclusions. The results suggest that use of the exchange led to a significant reduction in hepatitis B and hepatitis C in the county and may have also prevented a substantial proportion of human immunodeficiency virus infections in injection drug users. (*Am J Public Health.* 1995;85:1531–1537)

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Introduction

Each year, approximately 200 000 to 300 000 hepatitis B virus (HBV) infections and 150 000 hepatitis C virus (HCV) infections occur in the United States. Injection drug users are among those at highest risk for both types of viral hepatitis[1,2]; studies conducted in Europe and the United States with this population have found serologic evidence of HBV infection in 65% to 95% and evidence of HCV infection in 65% to 80%.[3–12] Although acute clinical hepatitis arising from infection with either virus usually resolves within several months, both hepatitis B and hepatitis C may result in persistent infection, chronic active hepatitis, cirrhosis, or primary hepatocellular carcinoma.[2,13]

Injection practices that transmit HBV or HCV may also transmit human immunodeficiency virus (HIV). In almost all developed countries outside the United States, syringe exchange programs and pharmacy sales of sterile injection equipment have become standard methods of preventing HIV transmission among injection drug users,[14–16] but these programs have remained extremely controversial in this country.[17–20] Evaluations of these programs have consistently suggested that they have produced reductions in HIV risk behaviors and no increases in the injection of illicit drugs.[21–25] Reductions in community incidence rates of HIV infection and hepatitis B among injection drug users have also been noted in association with syringe exchange programs.[26–30] To date, however, there have been no studies showing reduced individual exposure to bloodborne viruses linked to individual participation in syringe exchange programs, and studies of populations often cannot separate effects of exchange use from other concurrent interventions.

Because HIV, HBV, and HCV can be transmitted by sharing of drug injection equipment and because the incidence of hepatitis B and, probably, hepatitis C is commonly higher than that of HIV,[7,8,31] studies of HBV and HCV infections have been suggested as a method of evaluating HIV prevention programs.[32] A one-for-one syringe exchange program has been operating in Pierce County, Washington, since August 1988.[22] We report here on an individual-level association between use/nonuse of the syringe exchange and incident hepatitis B and C among injection drug users in Tacoma, Pierce County, Washington.

Methods

The Tacoma syringe exchange currently performs its duties in three stationary sites: two street-based exchanges that operate out of a van and a third exchange that is based in the county health department pharmacy. There is also a mobile exchange that serves injection drug users in outlying areas. These users are not

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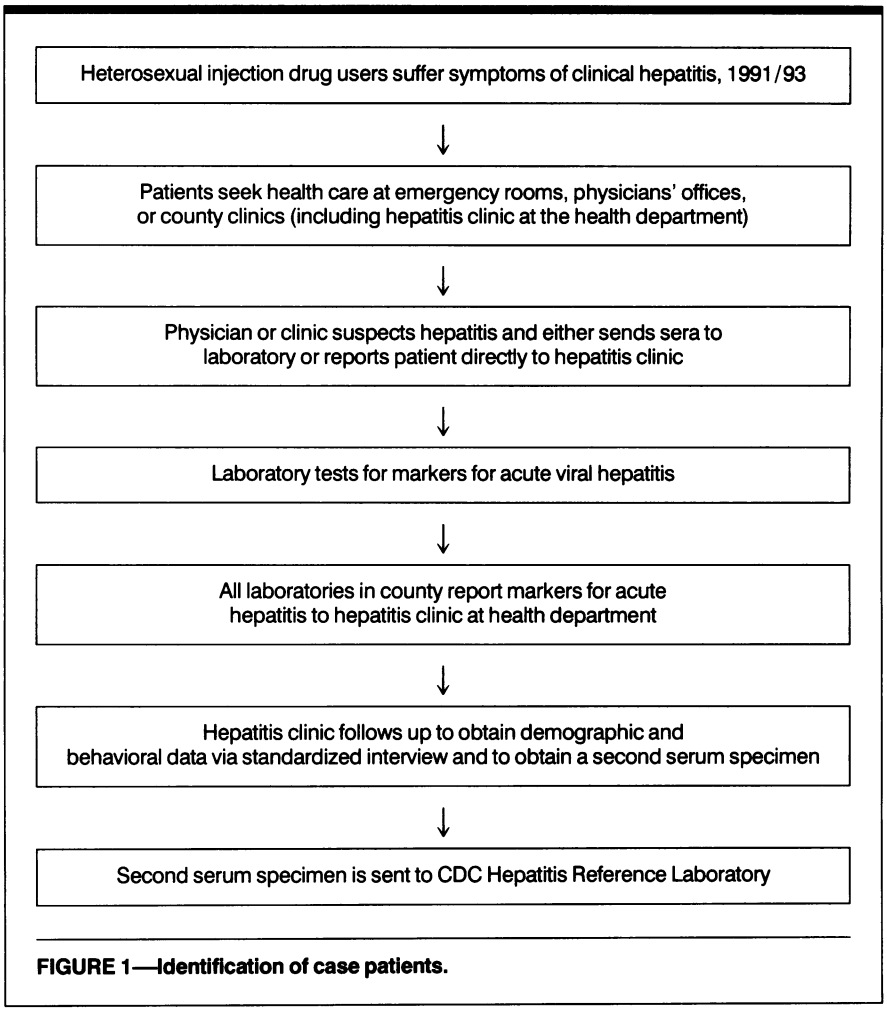

FIGURE 1—Identification of case patients.

required to register or show identification to participate in the program.

In addition to one-for-one syringe exchange, the program offers HIV-prevention education and risk reduction counseling, crisis intervention, and help in accessing medical and social services. Tuberculosis screening and directly observed therapy for persons who test positive for tuberculosis are also provided. Injection drug users participating in the program are offered disinfectant bleach, condoms, alcohol wipes, and other clean equipment (cookers and cotton) for drug injection. Pierce County, one of four US sentinel counties for acute viral hepatitis surveillance conducted by the Centers for Disease Control and Prevention (CDC), was the location of an outbreak of drug-related hepatitis B from 1985 to 1988. Incidence of hepatitis B in the county has fallen sharply since.[27]

Case and Control Patients

Criteria for diagnosis were established and data collection methods were executed according to the sentinel counties' protocol, with case patients being interviewed by public health nurses using a standardized questionnaire that included a supplemental question regarding syringe exchange use.[33,34] To meet the case definition for acute viral hepatitis, patients had to have had a discrete date of onset of clinical symptoms, serum aminotransferase levels greater than 2.5 times the upper limit of normal, and exclusion of other causes of liver injury. Hepatitis B was classified in patients who tested positive for hepatitis B surface antigen (HBsAg) and/or immunoglobulin M (IgM) antibody to hepatitis B core antigen (anti-HBc); hepatitis C was classified in patients who tested positive for antibody to HCV (anti-HCV) but negative for HBsAg, IgM anti-HBc, and IgM antibody to hepatitis A virus (anti-HAV). Figure 1 shows a flow diagram for case finding and data collection from potential case patients.

Thirty case patients who reported injecting drugs during the 6-month period prior to onset of clinical hepatitis met diagnostic criteria for hepatitis B, and 20 met criteria for hepatitis C. Two hepatitis B case patients who reported male-with-male sex were excluded, because they may have acquired hepatitis as a result of sexual contact rather than of sharing drug injection equipment. None of the remaining case patients reported other risk factors for hepatitis B or C, such as blood transfusion, health care employment with frequent blood contact, hemodialysis, or sexual or household contact with a confirmed case of hepatitis B or C during the previous 6 months.

Potential control subjects were 238 current injection drug users from either of two other Tacoma–Pierce County Health Department services (including those individuals entering a methadone drug treatment program or attending the HIV testing center) during the period when cases were reported (1991 to 1993). Data collection and control selection procedures are outlined in Figure 2. Potential control subjects who reported male-with-male sexual contact were excluded. To reduce possible bias in the estimation of exchange use, those who were referred by the syringe exchange to either the methadone treatment program or the HIV testing center were also excluded.

Demographic and behavioral data, without identifying information, were abstracted from clinical records (hepatitis surveillance system for case patients and methadone program and HIV testing center for control subjects). In each of the services that made up the study base, standard client information collected from injection drug users included demographic characteristics, syringe exchange use (recorded as ever vs never), duration of drug injection, sexual behavior information, and source of referral. Age was recoded as less than 25 years, 25 to less than 35 years, and 35 years and older. Race/ethnicity was reclassified as White or non-White, as there were too few non-White, non-African-American subjects to permit analysis within subgroups. A priori, onset of injection was defined as recent if it began less than 5 years prior to attendance in the health department clinic; this grouping was suggested by studies that indicated that the first 5 years of drug injection are associated with an increased risk of HIV transmission.[35,36]

Laboratory Testing

All laboratory testing was performed at the CDC Hepatitis Reference Laboratory. Cases of hepatitis B and hepatitis C were tested according to the sentinel counties' protocol.[33,37] Serum samples from patients with acute hepatitis were tested for HBsAg and total anti-HBc

using commercially available radioimmunoassays (Abbott Laboratories, Abbott Park, Ill), and were tested for IgM anti-HBc and IgM anti-HAV using enzyme immunoassays (Abbott Laboratories). Anti-HCV was detected by second-generation enzyme immunoassay (Abbott HCV EIA 2.0, Abbott Laboratories), and repeatedly reactive samples were tested by a supplemental anti-HCV immunoblot system (MATRIX HCV, Abbott Laboratories). For control subjects, sera remaining after routine serologic testing were tested for HBsAg, total anti-HBc, IgM anti-HBc, and anti-HCV as above.

Analysis

Risk factors for acute hepatitis B and C were examined separately. Odds ratios and their 95% confidence intervals (CIs) were used to determine whether subject characteristics (sex, race, age, duration of injection, and participation in syringe exchange) were associated with illness. The association between the exposure variable (nonuse of the syringe exchange) and hepatitis was examined within strata of potentially confounding variables (sex, race, age, and duration of injection). Woolf's test was used to detect heterogeneity of the odds ratios across strata.[38] After all potentially confounding variables were entered into a multiple logistic regression model, nonuse of the exchange was entered and a score statistic was calculated for the significance of the addition of this variable to the model.[39] The statistical significance of each variable's contribution to the model was determined by use of the Wald statistic, and 95% confidence intervals for the adjusted odds ratio for each variable were calculated.[40] Analysis was performed with SPSS for Windows and EGRET.[41,42]

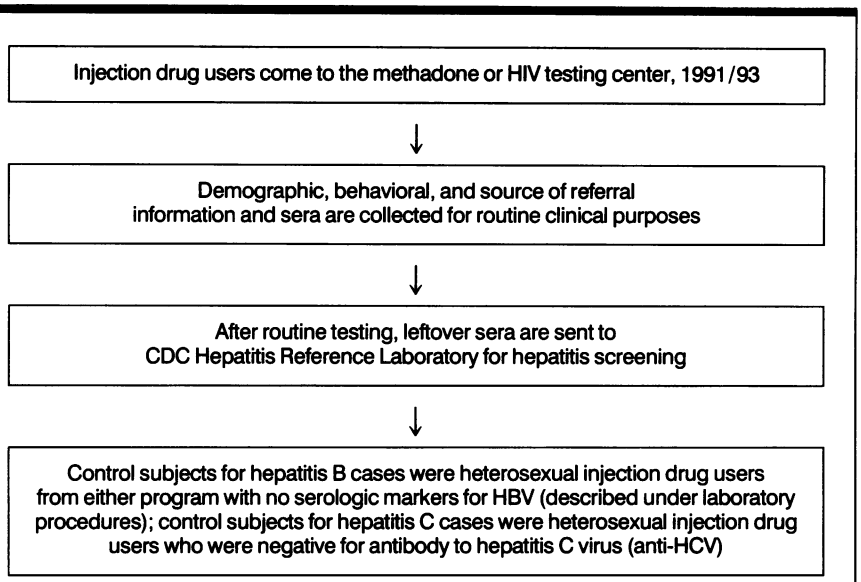

FIGURE 2—Identification of control subjects.

TABLE 1—Sex, Race, Age, and Duration of Injection Drug Use in Relation to Risk for Hepatitis B

	Case Patients (n = 28)		Control Subjects (n = 38)		Odds Ratio (95% Confidence Interval)
	No.	%	No.	%	
Sex					
Male	17	60.7	19	50.0	1.55 (0.52, 4.69)
Female	11	39.3	19	50.0	1.00
Race					
White	23	82.1	28	73.7	1.64 (0.43, 6.99)
Non-White	5	17.9	10	26.3	1.00
Age, y					
<25	11	39.3	5	13.2	13.20 (2.14, 95.32)
25–34	14	50.0	15	39.4	5.60 (1.19, 34.91)
35+	3	10.7	18	47.4	1.00
Years injecting[a]					
<5	13	48.1	8	21.1	3.48 (1.04, 11.96)
5+	14	51.9	30	78.9	1.00

[a]Data missing for one case patient.

Results

Of the study-eligible injection drug users, 28 with hepatitis B and 20 with hepatitis C were reported to the health department during the study period and completed the risk assessment interview. Two hundred thirty-eight injection drug users (204 entering methadone treatment and 34 attending an HIV testing clinic during the study period) were potential control subjects and were tested for hepatitis markers. Of these potential control subjects, 38 (16%) had no serologic evidence of HBV infection and 26 (11%) were anti-HCV negative. Additionally, all serologically eligible control subjects reported no male-with-male sexual contact or other risk factors for hepatitis B or C.

Hepatitis B

Almost 40% of the acute hepatitis B case patients were younger than 25 years old and 89% were younger than 35; 61% were male, and 82% were White (Table 1). Slightly more than half of the case patients reported injecting drugs for 5 or more years, and 75% had never used the syringe exchange (Table 2). There were minor differences between the case and control groups in the distributions of sex or race. However, compared with control subjects, injection drug users with hepatitis B were younger, had injected for fewer years, and were more likely to have never used the syringe exchange (Tables 1 and 2). In addition, 46% of injection drug users with hepatitis B were anti-HCV positive compared with 32% of controls ($P = .22$) (data not shown). Among both the case and control groups, younger persons and those injecting for less than 5 years were more likely to have never used the syringe exchange (Table 2).

TABLE 2—Odds Ratios (ORs) for the Association between Syringe Exchange Use and Risk of Hepatitis B, Unadjusted and within Strata of Sex, Race, Age, and Duration of Injection Drug Use

	Syringe Exchange Use	Case Patients (n = 28) No.	Case Patients (n = 28) %	Control Subjects (n = 38) No.	Control Subjects (n = 38) %	OR (95% Confidence Interval)
Unadjusted						
	Never	21	75.0	10	26.3	8.40 (2.43, 30.25)
	Ever	7	25.0	28	73.7	
Adjusted, by variable						
Sex						
Male	Never	11	64.7	4	21.1	6.88 (1.27, 41.26)
	Ever	6	35.3	15	78.9	
Female	Never	10	90.9	6	31.6	21.67 (1.99, 1010.24)
	Ever	1	9.1	13	68.4	
Race/ethnicity						
White	Never	18	78.3	8	28.6	9.00 (2.15, 40.60)
	Ever	5	21.7	20	71.4	
Non-White	Never	3	60.0	2	20.0	6.00 (0.35, 111.38)
	Ever	2	40.0	8	80.0	
Age, y						
<25	Never	9	81.8	3	60.0	3.00 (0.14, 56.28)
	Ever	2	18.2	2	40.0	
25-34	Never	10	71.4	5	33.3	5.00 (0.82, 32.78)
	Ever	4	28.6	10	66.7	
35+	Never	2	66.7	2	11.1	16.00 (0.48, 999.81)
	Ever	1	33.3	16	88.9	
Years injecting						
<5	Never	11	84.6	4	50.0	5.50 (0.50, 76.83)
	Ever	2	15.4	4	50.0	
5+	Never	9	64.3	6	20.0	7.20 (1.44, 37.54)
	Ever	5	35.7	24	80.0	

TABLE 3—Logistic Regression Analysis of the Risk of Hepatitis B and C: Adjusted Odds Ratios (AORs) and 95% Confidence Intervals (CIs)

Variable	Hepatitis B AOR	Hepatitis B 95% CI	Hepatitis C AOR	Hepatitis C 95% CI
Nonuse of the syringe exchange	5.53[a]	1.49, 20.44	7.29[a]	1.62, 32.75
Age <25 y	8.01	1.06, 60.62	4.01	0.89, 18.15
Age 25–34 y	4.12	0.83, 20.41	1.81	0.17, 19.17
Male	3.23	0.85, 12.42	1.47	0.27, 8.07
Injecting drugs <5 years	1.61	0.32, 8.06	1.36	0.21, 8.93
White	1.27	0.23, 6.95	1.07	0.19, 6.14

[a]Score test for the association of nonuse of the syringe exchange with risk of hepatitis B after adjustment for sex, age, race/ethnicity, and duration of drug injection: score statistic = 7.116, P = .008. Score test for the association of nonuse of the syringe exchange with risk of hepatitis C after adjustment for same covariates: score statistic = 7.543, P = .006.

The unadjusted odds ratio for the association between nonuse of the syringe exchange and hepatitis B was 8.40 (Table 2). None of the tests for heterogeneity of the odds ratios within strata of the covariates was statistically significant. When nonuse of the exchange was entered into a logistic regression model containing all the other demographic and drug use variables, the fit of the model was significantly improved (score test statistic [1 df] = 7.116, P = .008, Table 3), and the odds ratio for the association between nonuse of the syringe exchange and hepatitis B, adjusted for all other factors, was 5.53 (95% CI = 1.49, 20.44).

Hepatitis C

Twenty percent of the hepatitis C patients were younger than 25 years of age and 70% were younger than 35; 70% were male, 85% were White, and 35% had been injecting drugs for less than 5 years (Table 4). There were minor differences between case patients and control subjects in the distribution of sex, race, age, or duration of injection (Table 4); none of the control subjects and only 10% of the case patients were anti-HBc positive (P = .10). For the hepatitis C case patients, nonuse of the syringe exchange was not significantly more frequent among those younger than 25 or those who had been injecting for less than five years (Table 5).

Case patients were significantly more likely to have never used the syringe exchange program, and the unadjusted odds ratio for the association between nonuse of the exchange and hepatitis C was 8.14 (Table 5). Tests for the heterogeneity of odds ratios for the association between nonuse of the exchange and hepatitis C within strata of the covariates were not statistically significant. Addition of nonuse of the syringe exchange to a logistic regression model containing all potentially confounding variables significantly improved the fit of the model, with a 1-df score test statistic of 7.543, P = .006 (Table 3). After adjustment for all other variables, the odds ratio for the association between nonuse of the exchange and hepatitis C was statistically significant (adjusted odds ratio [AOR] = 7.29; 95% CI = 1.62, 32.75).

Discussion of Possible Bias

The source population for this study was injection drug users who resided in Pierce County and were at risk for developing hepatitis B or C. While some Pierce County injection drug users who contracted symptomatic hepatitis during the period of the study would not have been identified as hepatitis cases by the health department, their proportion of the total number of cases was probably unrelated to their use of the syringe exchange, so failure to include them in the study probably has introduced a very small bias at most. Because Pierce is a sentinel hepatitis surveillance county, the proportion of patients presenting with symptoms of hepatitis who are not reported is likely to be particularly low. Cases of asymptomatic HBV or HCV infection were unlikely to differ from

symptomatic cases with respect to characteristics related to drug injection practices or syringe exchange use.

In contrast, the control subjects selected in this study from the health department methadone treatment program and HIV testing center probably represent only a minority of injection drug users in Pierce County who were at risk for hepatitis but did not develop it. Plausibly, prior use of the needle exchange program is more common among the injection drug users chosen as control subjects for this study based on their proclivity to use public health programs than among potential controls who do not participate in public health programs. While some studies have found that injection drug users in drug treatment programs are less likely to report injection risk behavior than those sampled from health clinics or jail, others have noted that injection drug users who have never been in treatment are less likely to report risk behavior and that risk factors for HIV infection do not differ by treatment status.[43–45] However, the magnitude of the association is such that it is unlikely that the findings could be explained by selection bias.[46] Indeed, to negate the association between hepatitis and nonuse of the exchange, one would have to postulate a population of injection drug users among whom a very large proportion had never used the syringe exchange. In the case of hepatitis B, 238 potential control subjects represented about 8% of the estimated 3000 injection drug users in Pierce County, and 26% of these subjects had never used the syringe exchange. If there truly were no association between hepatitis B and nonuse of the exchange, 79% of the remaining 92% of potential control subjects would have to have never used the exchange ([.08 × .26] + [.92 × .79] = .75, the observed proportion of hepatitis B cases who never participated in the exchange.*) However, based on exchange program records and interview information regarding frequency of use, we

TABLE 4—Sex, Race, Age, and Duration of Injection Drug Use in Relation to Risk of Hepatitis C

	Case Patients (n = 20)		Control Subjects (n = 26)		Odds Ratio (95% Confidence Interval)
	No.	%	No.	%	
Sex					
Male	14	70.0	11	42.3	3.18 (0.80, 13.31)
Female	6	30.0	15	57.7	1.00
Race					
White	17	85.0	19	73.1	2.09 (0.39, 14.29)
Non-White	3	15.0	7	26.9	1.00
Age, y					
<25	4	20.0	4	15.4	2.00 (0.26, 14.93)
25–34	10	50.0	10	38.4	2.00 (0.45, 9.20)
35+	6	30.0	12	46.2	1.00
Years injecting					
<5	7	35.0	6	23.1	1.79 (0.41, 8.03)
5+	13	65.0	20	76.9	1.00

TABLE 5—Odds Ratios (ORs) for the Association between Syringe Exchange Use and Risk of Hepatitis C, Unadjusted and within Strata of Sex, Race, Age, and Duration of Injection Drug Use

	Syringe Exchange Use	Case Patients (n = 20)		Control Subjects (n = 26)		OR (95% Confidence Interval)
		No.	%	No.	%	
Unadjusted						
	Never	15	75.0	7	26.9	8.14 (1.83, 38.72)
	Ever	5	25.0	19	73.1	
Adjusted, by variable						
Sex						
Male	Never	10	71.4	3	27.3	6.67 (0.88, 56.73)
	Ever	4	28.6	8	72.7	
Female	Never	5	83.3	4	26.7	13.75 (0.94, 707.47)
	Ever	1	16.7	11	73.3	
Race/ethnicity						
White	Never	13	76.5	6	31.6	7.04 (1.32, 41.05)
	Ever	4	23.5	13	68.4	
Non-White	Never	2	66.7	1	14.3	12.06 (0.25, 821.99)
	Ever	1	33.3	6	85.7	
Age, y						
<25	Never	3	75.0	2	50.0	3.00 (0.08, 235.00)
	Ever	1	25.0	2	50.0	
25–34	Never	9	90.0	3	30.0	21.00 (1.39, 1047.84)
	Ever	1	10.0	7	70.0	
35+	Never	3	50.0	2	16.7	5.00 (0.34, 80.26)
	Ever	3	50.0	10	83.3	
Years injecting						
<5	Never	6	85.7	3	50.0	6.00 (0.27, 366.24)
	Ever	1	14.3	3	50.0	
5+	Never	9	69.2	4	20.0	9.00 (1.44, 66.41)
	Ever	4	30.8	16	80.0	

*This formula is the calculation of a weighted average, estimating the proportion of nonselected potential injection drug–using control subjects in Pierce County who would have to have never used the syringe exchange to obtain an odds ratio of 1.0 for the association between nonuse of the syringe exchange and hepatitis B. An odds ratio of 1.0 would be obtained if the same proportion of case patients as control subjects had never used the syringe exchange. For case patients, this proportion was 75% (see Table 2). We estimate that the 238 potential control subjects represented about 8% of the injection drug-using population of 3000, obtained by applying the National Institute on Drug Abuse (NIDA) estimate of the prevalence of illegal drug injection (0.5%) in the United States to the 1990 census of the Pierce County population.[47] Of the remainder of potential control subjects (92% of all injection drug users in the county), 79% would have to have never used the exchange to obtain 75% nonuse for the total injection drug-using population.

estimate that approximately 1000 to 1500 injection drug users (30% to 50% of the 3000 total injection drug users in the county) attend the program each week and that another 500 (17% of the county total) attend less often. Regular attendees would constitute a portion of all injection drug users who have ever used the syringe exchange, so it is likely that fewer than 33% to 53% of local injection drug users have never used the exchange program.

There may have been differences between case patients and control subjects in injection practices not measured in this study, and this may have resulted in uncontrolled confounding. Additionally, the case and control groups may have differed in their use of other strategies (e.g., disinfectant bleach, purchase of syringes in pharmacies) to prevent bloodborne viral infections, and this may have also contributed to the lower estimated risk of infection among exchange users; however, the syringe exchange is the primary local distributor of small bottles of disinfectant bleach for injection drug users, and pharmacy sale of syringes to persons suspected of illicit drug use is illegal in Washington state. As with any case–control study that collects data by interview, there may have been differences in reporting between case patients and control subjects, but there is no particular reason to believe that case patients would be likely to underreport ever having used the exchange. This study was not able to estimate the "effective dose" of syringe exchange, and the observed odds ratios may be viewed as a weighted average of dose-specific effects, weighted perhaps toward more frequent attendees who make up the majority of exchange users.

The Tacoma syringe exchange's role as the primary source of HIV prevention for local injection drug users may have contributed to the magnitude of the association between syringe exchange and risk of viral hepatitis in this study. It may also explain why studies of syringe exchange in Amsterdam, where there are more alternatives for acquiring sterile injection equipment, have found small or no effects.[48] Studies such as this one are probably also more relevant in the US context since syringe exchanges often exist in the presence of legal and practical barriers to other means of obtaining sterile injection equipment. The effect of syringe exchange participation may also be amplified by behavioral similarities within injection drug–user networks, such that the practice of using sterile injection equipment and other methods to prevent HIV infection is shared by one's injection drug–using associates, with the net result that syringe exchange use stands for a set of behaviors and characteristics that protect against infection.

Conclusions

If it is reasonable to assume that the case patients in this study were similar to all injection drug user cases in the population with respect to frequency of exposure (nonuse of the syringe exchange), we estimate that use of the syringe exchange would have led to a 61% reduction in hepatitis B and a 65% reduction in hepatitis C among local injection drug users.[49] Although injection-related hepatitis B incidence in the community may fluctuate for many reasons besides syringe exchange, the population-attributable risk percentage calculated here is consistent with the 75% reduction in injection-related hepatitis B in Pierce County observed after the syringe exchange program was implemented in Tacoma.[27]

Hepatitis B and hepatitis C appear to be reasonable proxies for HIV infection for several reasons: they are transmitted via the same route, have similar epidemiological features, and entail similar control efforts to reduce their incidence. Syringe exchange programs may therefore prevent a substantial proportion of new HIV infections in injection drug users, and, indirectly, reduce heterosexually and perinatally transmitted HIV infections as well. Early implementation and maintenance of effective HIV prevention programs for injection drug users in low (<5%) HIV-seroprevalence cities may have a particularly powerful effect by limiting the reservoir of HIV-positive injectors. These findings, which suggest that the Tacoma syringe exchange exerts a strong protective effect against bloodborne viral transmission, are consistent with the previously reported observations of safer injection by Tacoma syringe exchange participants.[22] Additionally, they support the recommendations of the National Commission on AIDS to provide syringe exchange and other legal access to sterile injection equipment for injection drug users.[50] □

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