



Published in final edited form as:

*Drug Alcohol Depend.* 2009 March 1; 100(3): 204–213. doi:10.1016/j.drugalcdep.2008.08.017.

## High Dead-Space Syringes and the Risk of HIV and HCV Infection among Injecting Drug Users

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### Abstract

This study examines the association between using and sharing high dead-space syringes (HDSSs)—which retain over 1,000 times more blood after rinsing than low dead-space syringes (LDSSs)—and prevalent HIV and hepatitis C virus (HCV) infections among injecting drug users (IDUs). A sample of 851 out-of-treatment IDUs was recruited in Raleigh-Durham, North Carolina, between 2003 and 2005. Participants were tested for HIV and HCV antibodies. Demographic, drug use, and injection practice data were collected via interviews. Data were analyzed using multiple logistic regression analysis. Participants had a mean age of 40 years and 74% percent are male, 63% are African American, 29% are non-Hispanic white, and 8% are of other race/ethnicity. Overall, 42% of participants had ever used an HDSS and 12% had shared one. HIV prevalence was 5% among IDUs who had never used an HDSS compared with 16% among IDUs who had shared one. The HIV model used a propensity score approach to adjust for differences between IDUs who had used an HDSS and those who had never used one. The HCV models included all potential confounders as covariates. A history of sharing HDSSs was associated with prevalent HIV (Odds Ratio = 2.50; 95% Confidence Interval = 1.01, 6.15). Use and sharing of HDSSs were also associated with increased odds of HCV infection. Prospective studies are needed to determine if sharing HDSSs is associated with increased HIV and HCV incidence among IDUs.

### Keywords

High dead-space syringes; Hepatitis C virus; HIV; Injecting drug users; Risk factors

### 1. Introduction

Wide variations in HIV prevalence among injecting drug users (IDUs) have been observed (Aceijas et al., 2004; Friedman et al., 2005) that are not fully explained by individual risk behaviors (Garfein et al., 2004). Structural factors (e.g., syringe access), network factors (e.g., rates at which HIV-negative IDUs engage in risk behaviors with HIV-positive IDUs), and biological factors (which influence the probability of transmission associated with an exposure)

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are likely to contribute to geographic variations in HIV prevalence among IDUs. For example, structurally, laws that restrict access to syringes and laws that criminalize possession of a syringe have been shown to increase the prevalence and frequency of syringe sharing (Bluthenthal et al., 1999; Heimer et al., 2002). Binge cocaine use has also been associated with increased frequency of syringe sharing (Wood et al., 2002). Laws that criminalize syringe possession have been associated with relatively anonymous sharing in settings like shooting galleries, contributing to high rates of mixing across different groups of IDUs (Rhodes et al., 2005).

Drug user network configuration has been shown to influence mixing patterns. For example, tightly knit networks of IDUs may operate as a protective factor while more loosely knit networks with many connection to other networks may increase risk (Friedman et al., 2000).

In regard to biological factors, laboratory studies, coupled with ethnographic observations, suggest that practices associated with the use of certain drugs, such as heating "black tar" heroin to dissolve it, may inactivate HIV, thus reducing the risk of HIV transmission when syringes are shared (Ciccarone and Bourgois, 2003; Clatts et al., 1999). Other biological factors, such as circumcision, have been shown to reduce the risk of HIV infection in men exposed through unprotected sex. (Bailey et al., 2007; Gray et al., 2007; 2008)

In contrast, the higher HIV viral loads associated with acute HIV infection have been shown to increase the risk of sexual transmission (Pilcher et al., 2004; 2007) Presumably receptive syringe sharing with an IDU during acute infection would result in exposure to more virus, which would increase the probability of HIV transmission associated with exposure via injection risk behaviors as well (Vickerman and Watts, 2002).

While a great deal has been learned regarding HIV transmission among IDUs over the past 25 years (Des Jarlais and Semaan, 2008), a number of unanswered questions remain, including inconsistent associations between HIV infection and injection risk behaviors (Garfein et al., 2004).

### 1.1 Hepatitis C virus

Unlike HIV, hepatitis C virus (HCV) infection has been consistently linked to risky injection practices, including receptive syringe sharing and sharing of drug preparation equipment (Thorpe et al., 2002). Although substantial variations in HCV prevalence (i.e., 2% to 100%) among IDUs around the world has also been observed, HCV prevalence among IDUs tends to be substantially higher than HIV prevalence (Hagan and Des Jarlais, 2000). The higher probabilities of transmission associated with injection-related exposures to HCV compared with HIV may contribute to these differences (Heimer, 1998).

### 1.2. Types of syringes used by IDUs

One potentially important factor that has received little attention is the type of syringes used by IDUs. Although most HIV transmission among IDUs is attributed to sharing needles and syringes (Normand, 1995), researchers rarely include behavioral survey questions that address the types of syringes used. This suggests that either all IDUs use the same type of syringe or that the type of syringe has no effect on risk. However, syringes used by IDUs vary in size and design, with some designs retaining substantially more blood after use than others (Gaughwin et al., 1991; Grund et al., 1996; Zule et al., 1997; 2002).

The types of syringes (i.e., size and design) used by IDUs in a given geographic area vary according to availability, local preferences, and cultural practices. The relative importance and stability of these factors has rarely been described in published reports. However, there is evidence that under certain circumstances, changes in availability can be an important

determinant. For example, in Texas, during the 1970s and 1980s, pharmacies stopped selling insulin syringes with detachable needles and began selling fixed-needle insulin syringes (Zule et al., 2002). Although some IDUs preferred the detachable needle syringes, the fixed-needle syringes met their needs and they were relatively easy to obtain. Consequently, there was no large demand for detachable needle syringes and they were phased out almost completely. Similarly a study of injecting practices in prisons suggests that IDUs will use makeshift equipment as well as any type of needle and syringe that they are able to obtain (Seamark and Gaughwin, 1994). However, in areas where IDUs inject drugs that require volumes of water greater than 1 milliliter (ml), it may be difficult to persuade IDUs to switch to 1 ml syringes, regardless of design. Therefore, recommendations for syringe exchange programs stress the importance of providing IDUs with syringes that they prefer and that meet their needs (Burrows, 2007).

### 1.3. Syringe design and fluid retention

When the plunger is fully depressed, all syringes retain fluid in what has been termed “dead-space” (Strauss et al., 2006). In high dead-space syringes (HDSSs)—which usually have detachable needles—when the plunger is fully depressed, fluid is retained in the tip of the syringe, the hub of the needle, and the needle itself. In contrast, low dead-space syringes (LDSSs) have a needle—which is usually permanently attached—that extends through the tip of the syringe to the base of the syringe barrel. With the plunger fully depressed, LDSSs only retain fluid in the needle itself.

Experiments have shown that 1 ml high dead-space insulin syringes with 26-gauge 0.5-inch detachable needles retain approximately 84 microliters ( $\mu\text{l}$ ) of fluid with the plunger fully depressed. In contrast, 1 ml low dead-space insulin syringes with 28-gauge permanently attached needles retain approximately 2  $\mu\text{l}$  of fluid (Zule et al., 1997). Furthermore, in experiments that simulated registering (i.e., drawing blood into the syringe to confirm it is in a vein) with 0.1 ml of blood, injection, booting or flushing (i.e., drawing blood into a syringe and reinjecting it to rinse residual drug solution out of the dead-space after the contents have been injected) with 0.1 ml of blood and two 0.5 ml rinses with water, HDSSs retained approximately 1  $\mu\text{l}$  of blood and LDSSs retained  $<0.001$   $\mu\text{l}$  (Zule et al., 1997; 2002).

### 1.4 HIV infection following exposure

The difference in the amount of blood retained may be an important factor because the probability of HIV infection following an exposure is related to the amount of blood and virus in the exposure. Clear evidence for this is found in the low rates of HIV seroconversion following exposure through accidental needlesticks and the high rates of seroconversion following blood transfusions (Baggaley et al., 2006). The volume of blood and virus in an exposure has been shown to be one of the most important predictors of HIV seroconversion following occupational exposures through accidental needlesticks and other percutaneous exposures among healthcare workers (Cardo et al., 1997; Gerberding, 1994). Moreover, laboratory studies have found that the volume of residual blood in a used syringe is an important predictor of whether HIV could be cultured from it (Abdala et al., 1999; 2000). Higher viral loads also have been shown to increase the probability of perinatal and sexual transmission (Giaquinto et al., 2005; Wawer et al., 2005).

Because HDSSs, after they are rinsed with water, retain over 1,000 times more blood than LDSSs, it seems likely that the probabilities of HIV and HCV transmission would be substantially greater when HDSSs are shared than the probabilities of transmission associated with sharing LDSSs. The difference between the 1 $\mu\text{l}$  of blood in an HDSS and the 0.001  $\mu\text{l}$  of blood retained in an LDSS may cross an important threshold. For example, at a moderately high HIV viral load set-point of 100,000 copies per ml (Fraser et al., 2007) there is only a 1-

in-10 probability that an LDSS would contain a single copy of HIV. In contrast, we would expect each HDSS to contain an average of 100 copies of HIV. For HCV at a moderate viral load of 500,000 copies per ml there is a 1-in-2 probability of an LDSS containing a single copy of HCV. In contrast, we would expect each HDSS to retain an average of 500 copies of HCV.

Therefore, we hypothesized that prevalence of HIV and HCV would be higher among IDUs who reported a history of sharing HDSSs than among IDUs who had never shared or used them. This report presents exploratory findings examining associations between using and sharing HDSSs and prevalent HIV and HCV infection. It focuses on determining if the evidence is consistent with the biologically plausible hypothesis that sharing HDSSs is associated with prevalent HIV and HCV infection.

## 2. Methods

### 2.1 Background and setting

Data analyzed in this report were collected as part of an intervention study to reduce alcohol use, injection-related risk behaviors, and sexual risk behaviors among IDUs in the metropolitan area of Raleigh-Durham, North Carolina (Zule et al., In press). Although the study included follow-up interviews at 6-months and 12-months after enrollment to assess intervention effects, only baseline data were analyzed for this report. At the time of the study, there were no syringe exchange programs in the Raleigh-Durham area. However, pharmacy sales of syringes were and are permitted; although pharmacy regulations stipulate that pharmacists should use their professional judgment in deciding to whom to sell syringes (North Carolina Administrative Code, 2007).

As in many other states that permit pharmacy sales of syringes, legally purchased syringes may become “drug paraphernalia” after an IDU leaves the store (McNeely et al., 2006; Reich et al., 2002; Simpson, 2002). In North Carolina, the drug paraphernalia law stipulates that factors such as prior convictions of the syringe owner or presence of a controlled substance are considered in determining whether a syringe constitutes drug paraphernalia (North Carolina General Statutes, 1994).

### 2.2 Participants

Using a targeted sampling approach that has been used in other cities (Carlson et al., 1994; Watters and Biernacki, 1989), a total of 851 out-of-treatment IDUs were enrolled in the study between July 2003 and January 2006 in the Raleigh-Durham metropolitan area. This approach included street outreach methods, where former drug users go into high drug use communities to recruit active drug users and distribute risk-reduction materials (e.g., condoms, bleach, water, and educational materials) (Cunningham-Williams et al., 1999). It should be noted that HIV intervention research and prevention service activities (e.g., education, early bleach distribution, condom distribution, HIV counseling and testing) targeting IDUs and noninjecting crack users in this area have been active since at least 1994. After preliminary field screening, prospective participants were referred to a project office where they were screened for eligibility, the study was described to them, and they provided informed consent.

To minimize underreporting of sensitive behaviors, data collection was performed using Audio Computer-Assisted Self-Interviewing (ACASI) technology (Metzger et al., 2000). After completing the initial interview, participants were randomized to either a motivational intervention or an educational intervention. Following the first intervention session, participants were offered counseling and testing for antibodies to HIV and HCV. Participants received their test results and posttest counseling approximately one week later. Follow-up

interviews were scheduled for 6 and 12 months after enrollment to evaluate intervention effects. However, only baseline data were analyzed for this report.

The HIV model is restricted to the 791 participants that had valid HIV test results and provided complete data on all of the items used in the analyses. The HCV model is restricted to the 750 participants who had valid HCV test results and provided complete data on all of the items used in the analyses. More of the participants were tested for antibodies to HIV than HCV because the HIV test only required an oral swab and the HCV test required a blood sample, and there was a brief period when there was no phlebotomist at one field site.

Eligibility criteria for the study included the following: a minimum age of 18 years; self-reported injecting drug use in the previous 30 days; visible tracks (injection marks) and/or a urine specimen positive for heroin (morphine), cocaine, or methamphetamine; no formal substance abuse treatment in the previous 30 days; and current residence in one of the two counties (Durham or Wake County) in which the study was conducted. This study was approved by RTI International's Office for Research Protection.

### 2.3 Measures

Participants were screened for HIV antibodies using the Orasure HIV-1 ELISA test (Orasure Technologies, Bethlehem, PA). Specimens that were reactive on two ELISAs were confirmed by Orasure Western Blot. Participants were screened for HCV antibodies using the HCV EIA test (Orthoclinical Diagnostics, Rochester, NY) with a signal to cutoff ratio of  $>8$ . Specimens with a signal to cutoff ratio  $<8$  were confirmed using qualitative polymerase chain reaction (PCR). PCR testing was used to confirm infection in specimens with marginal levels of antibodies, not to confirm active infection.

Use and sharing of HDSSs were assessed by the following items: (1) Have you ever used a syringe with a needle that comes off? (2) When was the last time you used a syringe with a needle that comes off? (3) How many times in the past 30 days did you use a syringe with a needle that comes off? (4) Have you ever used a syringe with a needle that comes off that had been used by somebody else? (5) When was the last time that you used a syringe with a needle that comes off that had been used by somebody else? (6) How many times in the past 30 days did you inject with a needle that comes off that had been used by somebody else? (7) Where did you get the syringe with a needle that comes off the last time you used one? and (8) Why did you use a syringe with a needle that comes off the last time you used one?

A history of (receptive) syringe sharing was assessed with the question, "When was the last time you used works (needles/syringes) that you know had been used by somebody else?" A response of "never" was coded as never shared and all other responses were coded as ever shared.

In addition to (receptive) syringe sharing, a variety of other injection practices have been identified that may introduce blood at different points in the drug preparation process. These practices have been labeled indirect sharing and syringe-mediated drug sharing (Grund et al., 1996; Koester et al., 2005; Zule, 1992), and they have been identified as risk factors for HCV incidence among IDUs (Hagan et al., 2001; Hahn et al., 2002; Maher et al., 2006; Thorpe et al., 2002).

A history of indirect sharing or syringe-mediated drug sharing was derived from three variables: (1) When was the last time that you used a cotton, cooker, spoon, or water (for rinsing or mixing) that had been used by somebody else? (2) When was the last time that you injected drugs that were mixed with water that was added from a syringe that you know had been used

by somebody else? and (3) When was the last time that you injected drugs that had been drawn up into somebody else's syringe to measure or divide?

If a participant reported never engaging in any of these practices, indirect sharing was coded as no indirect sharing ever. Using a cooker, cotton, spoon, or water that had been used by someone else would, in most instances, result in exposure to less blood than syringe-mediated drug sharing (i.e., adding water with a used syringe or using a used syringe to measure and divide liquefied drugs). Therefore, we distinguished between people who had only used a cooker, cotton, or water after someone else and those who reported syringe-mediated drug sharing. Thus, we created an indirect sharing hierarchy based on lifetime behaviors: (1) no indirect or syringe-mediated drug sharing, (2) indirect sharing but no syringe-mediated drug sharing, and (3) syringe-mediated drug sharing.

We also created a classification of injection risk with five mutually exclusive categories, which were based on lifetime behaviors: (1) Never used an HDSS and never shared any type of syringe; (2) Never used an HDSS, but shared an LDSS; (3) Used an HDSS, but never shared any type of syringe; (4) Used an HDSS and shared an LDSS; and (5) Used and shared an HDSS.

## 2.4 Analyses

In our observational study, the subjects were not randomized with respect to the use of HDSSs and LDSSs. Therefore, in the analysis we needed to adjust for nonrandom assignment. We used a propensity score approach to adjust for potential bias in our model examining associations between using and sharing each type of syringe and prevalent HIV infection (D'Agostino, 1998; Rosenbaum and Rubin, 1983). Additional justification for the use of propensity scoring comes from the fact that the number of HIV-positive subjects is relatively small and the inclusion of a number of control variables would leave little power for the estimates. Thus, the essence of propensity score modeling is twofold: the inclusion of a surrogate variable that encapsulates a number of risks associated with the outcome, and bias compensation for the nonrandomized design. We included variables that were associated with the outcome (i.e., HIV status) in this sample, variables that have been routinely associated with HIV in other studies, and variables associated with the exposure (i.e., ever used a dead-space syringe) that could plausibly be associated with HIV status. We considered excluding variables from the propensity score calculation that were associated with a history of using an HDSS but not with HIV status, as recommended by Brookhart et al. (2006). However, there were no variables that clearly met those criteria, so following the recommendations of Rubin and Thomas (1996), all variables associated with a history of using an HDSS or with HIV were included in calculating the propensity score.

Therefore, the analysis model has the form:

$$\text{Logit}(U) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \dots + \beta_m X_m,$$

where  $U$  is the probability of using an HDSS,  $\beta_i$  are regression parameters and  $X_i$  are the variables in the propensity model. The analysis model then becomes:

$$\text{Logit}(Y) = \gamma_0 + \gamma_1 U + \gamma_2 V,$$

where  $Y$  is the probability of being HIV positive, and  $\gamma$  is the propensity of using the syringe.

Variables that were included in the propensity score calculations were age, gender, race/ethnicity, self-reported sexual orientation, ever being in prison, self-reported history of a

sexually transmitted infection (i.e., gonorrhea, chlamydia, syphilis, genital warts or genital herpes), year of first injection, number of years since first injection, a history of indirect sharing (i.e., sharing cookers, cottons, or rinse water), a history of syringe-mediated drug sharing (i.e., using a used syringe to add water to powder/solid drugs or divide liquefied drugs), and primary source of syringes (pharmacy vs. other). Drug use variables included use of cocaine, heroin, or methamphetamine in the previous 30 days. Sexual risk behaviors included trading sex for money or drugs in the previous 30 days, giving money or drugs for sex in the previous 30 days, engaging in unprotected intercourse in the previous 30 days, and reporting more than one sexual partner in the previous 30 days. Histories of substance abuse treatment, such as methadone detoxification treatment, methadone maintenance treatment, and treatment for cocaine use, were included because they differed substantially between participants who had used HDSSs and those who had never used them. We also included recruitment site to adjust for any unmeasured differences between IDUs recruited in Raleigh and in Durham. All of the variables included had shown significant association with the outcome in this study (or in other studies) and the exposure.

Predicted probabilities (i.e., the propensity score) of using an HDSS in the initial model were entered as a covariate in a multiple logistic regression model that examined associations between using and sharing HDSSs and HIV status. The distribution of the propensity scores was unimodal, which indicates a high level of smoothing.

Because of the large numbers of HCV-positive and HCV-negative participants, we included all potential risk factors in a multiple logistic regression analysis, as recommended by Cepeda et al. (2003) rather than using a propensity score approach. This approach accounts for the nonrandomness in syringe assignment as well as directly estimating the effects of individual factors associated with being HCV positive.

We also used multiple logistic regression analysis to assess the possible association between engaging in indirect sharing and syringe-mediated drug-sharing practices using HDSSs and HCV infection among people that reported never sharing any type of syringe. This model included interactions between indirect sharing practices (i.e., sharing cookers, cottons, and rinse water) that may involve relatively small volumes of liquid and blood, syringe-mediated drug-sharing practices that are likely to involve exposure to larger volumes of blood and use of HDSSs.

### 3. Results

#### 3.1 Characteristics of the sample

Among study participants, HIV prevalence was about 8% and HCV prevalence was about 54%. Heroin, powder cocaine, and crack cocaine were the most commonly used drugs. Less than half of participants had ever shared a syringe, and less than one fifth had shared a syringe in the previous 30 days. Over half reported a history of at least one indirect sharing or syringe-mediated drug-sharing practice and approximately one quarter reported one of these practices in the previous 30 days. Among participants, 42% reported ever using an HDSS and nearly 20% reported using one in the previous 30 days, and about 13% had ever shared an HDSS and about 5% had shared one in the previous 30 days. Additional details regarding the sample are shown by a history of using HDSSs in Table 1.

#### 3.2 HIV model

In the multiple logistic regression model that included the propensity score as a covariate, participants who reported a history of using and sharing an HDSS were significantly more likely to be HIV-positive (Odds Ratio [OR] = 2.50; 95% Confidence Interval [CI] = 1.01, 6.15)

than participants that had never shared any type of syringe and never used an HDSS. Sharing LDSSs was not associated with prevalent HIV infection. Table 2 presents the bivariate and multiple logistic regression models for HIV.

### 3.3 HCV model

In both bivariate and multiple logistic regression analyses, older age, homelessness, longer history of injection, a history of methadone maintenance, obtaining syringes from pharmacies, a history of indirect sharing, and using and sharing HDSSs were all associated with increased odds of prevalent HCV infection. In multiple logistic regression analyses, use of an HDSS among IDUs who had never shared syringes (OR = 2.25; 95% CI = 1.30, 3.90), using HDSS and sharing LDSS (OR = 2.85; 95% CI = 1.43, 5.69), and using and sharing HDSS (OR = 2.21; 95% CI = 1.12, 4.35) were all associated with increased odds of HCV infection compared with participants who had never used an HDSS or shared any type of syringe. Table 3 presents the bivariate and multiple logistic regression models for HCV.

Table 4 presents the results of the bivariate and multiple logistic regression models for HCV infection among people that denied a history of syringe sharing. The interaction between a history of syringe-mediated drug sharing and using an HDSS was significantly associated (OR = 6.42; 95% CI = 1.56, 26.37) with HCV infection, while adjusting for other potential confounders.

### 3.4 Sources of HDSSs and reasons for using them

Of the 194 participants who had used an HDSS since 2000, 41% reported obtaining it from a pharmacy the last time they used one, 33% from a friend or relative, 16% from a syringe seller or drug dealer, and 10% from other sources. Among participants, 62% reported last using an HDSS because it was the easiest to obtain, 17% reported that they preferred HDSS, and 21% reported other reasons for using an HDSS.

## 4. Discussion

The independent association observed between a history of sharing HDSSs and prevalent HIV infection is consistent with the biologically plausible hypothesis that sharing HDSSs is more risky than sharing LDSSs. Likewise, the independent association between using and sharing HDSSs and prevalent HCV infection is consistent with the hypothesis that sharing HDSSs increases risk for HCV infection as well. The significant interaction between syringe-mediated drug sharing and a history of using HDSSs and HCV infection among people that denied a history of receptive syringe sharing is consistent with our hypothesis as well.

While none of the findings in this study approach the level of evidence needed to establish a *causal* relationship between sharing HDSSs and increased HIV and HCV transmission, they are consistent with the biologically plausible hypothesis. Moreover, these findings are consistent with a previous study (Zule et al., 2002) that found an association between a history of using HDSSs and prevalent HIV infection. The key hypothesis behind the evidence presented is based on the premise that the probability of transmission associated with an exposure is influenced by the viral burden (i.e., viral load  $\times$  volume of inoculum) in the exposure. Similar to sex risk behaviors, the risks of HIV transmission associated with direct and indirect syringe sharing are influenced by a number of factors, and the protective role of LDSSs may be analogous to the role of male circumcision or antiretroviral therapy. While circumcision and antiretroviral therapy do not eliminate HIV transmission risk, evidence suggests that they reduce the probability of transmission associated with an exposure (Cohen et al., 2008; Hallett et al., 2008; Johnson and Quinn, 2008).



In addition to reducing the risk of infection among individuals, ecological evidence from sub-Saharan Africa suggests that circumcision may have a population effect as well. It has been shown that circumcision rates in African countries are highly correlated with HIV prevalence rates (Auvert et al., 2001; Drain et al., 2006). This raises the question whether or not variations in the percentage of IDUs using HDSSs in an area could partially explain some of the observed geographic variations in HIV prevalence. Because the probability of transmission associated with injection-related exposures (e.g., receptive syringe sharing) is a critical parameter in mathematical models of HIV epidemics among IDUs (Grassly et al., 2003; Kaplan and Heimer, 1992), it seems likely that the widespread use of HDSSs in a given area would amplify the effects of commonly accepted risks, such as frequency of receptive syringe sharing and sharing across networks.

This study also provides additional evidence that even in the United States, where it is generally assumed that all IDUs use LDSSs (Lurie et al., 1993; Zule et al., 2002), many IDUs have used HDSSs and some continue to do so.

#### 4.1 Limitations

Several limitations should be considered when interpreting these findings. First, a causal relationship between using and sharing HDSSs and prevalent HIV and HCV infection cannot be established from a cross-sectional study such as this. However, most risk factors for HIV among IDUs were originally identified in cross-sectional studies before they were included in longitudinal incidence studies. The fact that a biologically plausible risk factor has not been studied systematically is not evidence that it is not a risk factor.

Second, as with most studies of injecting and sex risk behaviors, this study relies on self-reports that may be subject to faulty recall or intentional misreporting. In addition, many of the lifetime behaviors may be particularly sensitive to faulty recall. However, data were collected via ACASI to minimize underreporting of sensitive and potentially embarrassing behaviors. Despite these efforts, we cannot rule out these potential sources of error. However, there is no reason to suspect that recall and intentional misreporting would differ systematically between people who had used HDSSs and those who had never used them. If there is no systematic bias, then faulty recall and underreporting would be sources of error variance that would reduce power without changing the direction of the results. For example, while the percentage of participants that reported never engaging in any type of injection risk behavior (e.g., direct or indirect sharing of syringes or syringe-mediated drug sharing) seems somewhat high, there is no readily apparent reason why people who had only used LDSSs would be systematically more likely to underreport injection risk than people who had used HDSSs.

Third, no sampling frame exists for IDUs, so it is not possible to assess the representativeness of the sample. Although targeted sampling was used to ensure a more diverse sample, street outreach methods tend to reach drug users who hang out on the street. Therefore, employed drug users and mid- to upper-level drug dealers may be underrepresented in this sample and caution should be used in generalizing these findings to other groups of drug users.

One final point is that the associations between a history of methadone maintenance treatment and obtaining syringes from pharmacies and HCV in the models should be interpreted cautiously because these variables were also associated with longer histories of injection and heavier drug use in this sample.

#### 4.2 Conclusions

Despite these limitations, this is the first study to link using and sharing HDSSs with prevalent HIV and HCV infection, while adjusting for other potentially important risk factors. In order

to establish a causal association between HDSSs and incident HIV and HCV infections, prospective studies are needed in geographic areas where HIV and HCV incidence are high among IDUs and both types of syringes are commonly used. In the meantime, it may be helpful if researchers studying HIV and HCV among IDUs included questions on the types of syringes used and shared by IDUs to see if these results can be replicated. These data would also make it possible to determine if there is a correlation between HIV prevalence among IDUs in an area and the percentage of IDUs using HDSSs. If future studies confirm the associations between HDSSs and HIV and HCV infection, efforts to reduce the use of HDSSs could be a target for individual behavioral and structural interventions.

Interventions to reduce the use of HDSSs and increase the use of LDSSs may require significant policy debates regarding the distribution of syringes via syringe exchange programs where the type of syringes distributed can be controlled versus unrestricted pharmacy sales. The findings from this study will help to inform that debate and prompt additional research into the potential roles of HDSSs and LDSSs in HIV and HCV epidemics among IDUs.

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**Table 1**  
Characteristics of the study sample

	Total (n=822)	Ever used a high dead-space syringe	
		No (n=477)	Yes (n=345)
Background characteristics			
Mean Age (S.D.) ***	40.4 (9.4)	38.3 (9.3)	43.3 (8.7)
% Male	74.0	71.7	77.1
Race/ethnicity			
African American	63.9	63.7	64.3
Non-Hispanic white	28.4	29.0	27.5
Other	7.7	7.4	8.1
% Completed high school	68.9	68.1	69.9
% Unemployed	70.9	71.5	70.1
% Homeless	35.8	34.7	37.4
% Married or living as married	19.3	18.2	20.9
% Ever in substance abuse treatment ***	76.2	71.8	82.3
% Ever in methadone detoxification treatment ***	20.0	14.2	28.1
% Ever in methadone maintenance treatment ***	24.0	20.5	28.9
% Ever treated for cocaine use	43.7	43.4	44.1
% Ever in prison **	55.7	51.7	61.3
% History of sexually transmitted infection ***	48.2	43.4	54.8
% HIV positive ***	7.8	5.0	11.6
% HCV positive ***	53.4	40.8	70.9
Drug use past 30 days			
% Drank alcohol	71.5	70.6	72.8
% Used crack cocaine	73.3	71.8	75.5
% Used powder cocaine	64.7	62.4	67.8
% Used heroin ***	69.3	64.4	75.9
% Used methamphetamine **	11.7	9.2	15.2
Injecting practices lifetime and past 30 days			
Mean # of years since first injection (S.D.) ***	18.0 (12.2)	14.5 (11.2)	22.6 (12.0)
Mean # of injections past 30 days (S.D.)	28.1 (49.9)	28.6 (46.8)	27.4 (53.9)
Mean # of times shared a syringe past 30 days (S.D.)	1.6 (10.2)	1.7 (11.6)	1.4 (7.9)
Mean # of times used an HDSS past 30 days (S.D.)	1.9 (8.8)	0.0	4.6 (13.3)
Mean # of times shared an HDSS past 30 days (S.D.)	0.81 (9.9)	0.0	1.9 (15.3)
Year of first injection ***			
≤ 1970	11.9	6.6	19.4
1971–1980	21.4	14.4	31.1
1981–1990	25.1	25.6	24.3
1991–2000	26.0	32.4	17.0
≥ 2001	15.6	21.0	8.2
% Receptive syringe sharing (lifetime) ***	46.1	36.7	59.1

	Total (n=822)	Ever used a high dead-space syringe	
		No (n=477)	Yes (n=345)
% Receptive sharing past 30 days	17.2	16.8	17.7
% Pharmacy primary source of syringes	57.5	55.8	59.9
Indirect sharing/syringe-mediated drug-sharing practices lifetime ***			
% Never any type of indirect sharing or syringe-mediated drug sharing	46.1	36.7	59.1
% Shared cookers, cottons or rinse water, but never any type of syringe-mediated drug sharing	7.5	8.0	7.0
% Syringe-mediated drug sharing	46.4	37.5	-58.6
% Shared cookers cottons, or water past 30 days	24.9	23.1	27.5
% Shared liquefied drug solution past 30 days	23.1	20.8	26.4
% Used an HDSS lifetime	42.0	0.0	100.0
% Used an HDSS past 30 days	18.3	0.0	44.5
% Shared an HDSS lifetime	13.2	0.0	32.4
% Shared an HDSS past 30 days	4.7	0.0	11.1
Sexual practices and risk			
% >1 Sex partner past 30 days	27.3	28.3	25.9
% Unprotected intercourse past 30 days	37.3	36.9	38.0
% Traded sex for drugs or money past 30 days	16.2	16.2	16.1
% Traded drugs or money for sex past 30 days	24.9	23.8	26.5

\* p < 0.05

\*\* p < 0.01

\*\*\* p < 0.001

**Table 2**  
Bivariate and multiple logistic regression models for HIV

	Bivariate logistic regression		Multiple logistic regression	
	Odds ratio (95% confidence interval)	p-value	Adjusted odds ratio (95% confidence interval)	p-value
Predicted probability of using an HDSS* (propensity score)	10.37 (2.80, 38.34)	<0.001	4.76 (1.04, 21.81)	0.045
Use and sharing of LDSSs** and HDSSs		0.003		0.236
Never shared syringes and never used an HDSS	Ref		Ref	
Shared LDSS but never used an HDSS	1.08 (0.44, 2.66)	0.869	0.89 (0.34, 2.33)	0.808
Used an HDSS but never shared any type of syringe	1.92 (0.82, 4.51)	0.134	1.50 (0.60, 3.77)	0.383
Used an HDSS and shared an LDSS	2.44 (1.06, 5.63)	0.036	1.40 (0.53, 3.73)	0.500
Used and shared HDSS	4.02 (1.88, 8.61)	<0.001	2.50 (1.01, 6.15)	0.047

\* HDSS = high dead-space syringe

\*\* LDSS = low dead-space syringe



**Table 3**  
Bivariate and multiple logistic regression models for HCV

	Bivariate logistic regression		Multiple logistic regression	
	Odds ratio (95% confidence interval)	p-value	Adjusted odds ratio (95% confidence interval)	p-value
Age	1.09 (1.07, 1.11)	< 0.001	1.06 (1.03, 1.09)	< 0.001
Race/ethnicity		0.216		0.203
Non-Hispanic white	Ref	—	Ref	—
African American	0.82 (0.60, 1.13)	0.225	0.66 (0.41, 1.04)	0.074
Other	0.62 (0.35, 1.10)	0.103	0.76 (0.35, 1.61)	0.466
Male	1.10 (0.80, 1.52)	0.561	0.97 (0.63, 1.50)	0.900
Recruited in Raleigh	0.72 (0.54, 0.97)	0.029	0.64 (0.43, 0.96)	0.030
Homeless	0.60 (0.45, 0.81)	0.001	0.61 (0.42, 0.91)	0.015
Ever in prison	1.58 (1.18, 2.10)	0.002	1.15 (0.78, 1.70)	0.471
Ever in methadone maintenance	3.12 (2.18, 4.49)	< 0.001	2.28 (1.44, 3.60)	< 0.001
Ever had a sexually transmitted infection	1.30 (0.99, 1.72)	0.063	0.96 (0.66, 1.40)	0.847
Number of injections past 30 days	1.01 (1.00, 1.01)	0.009	1.00 (1.00, 1.01)	0.053
Pharmacy primary source of syringes	1.94 (1.44, 2.59)	< 0.001	1.84 (1.24, 2.72)	0.002
Years since first injection		< 0.001		0.001
0–5	Ref	—	Ref	—
6–10	1.72 (1.02, 2.90)	0.043	1.56 (0.83, 2.90)	0.165
11–15	2.27 (1.30, 3.97)	0.004	1.90 (0.97, 3.71)	0.061
16–20	2.15 (1.29, 3.60)	0.004	1.57 (0.83, 2.99)	0.166
21–25	7.04 (3.94, 12.57)	< 0.001	4.27 (2.05, 8.90)	< 0.001
26–30	7.65 (4.23, 13.82)	< 0.001	3.64 (1.68, 7.88)	0.001
31–35	15.93 (8.00, 31.60)	< 0.001	5.07 (2.10, 12.27)	< 0.001
>35	12.38 (5.90, 26.00)	< 0.001	5.59 (2.03, 15.42)	0.001
Indirect sharing/syringe-mediated drug-sharing practices lifetime		< 0.001		0.006
Never any type of indirect sharing or syringe-mediated drug sharing	Ref	—	Ref	—
Shared cookers, cottons, or rinse water but never any type of syringe-mediated drug sharing	1.99 (1.15, 3.45)	0.014	2.4 (1.17, 4.93)	0.017
Syringe-mediated drug sharing	2.42 (1.79, 3.26)	< 0.001	2.02 (1.24, 3.30)	0.005
Use and sharing of LDSSs* and HDSSs**		< 0.001		< 0.001
Never shared syringes and never used an HDSS	Ref	—	Ref	—
Shared LDSS but never used an HDSS	1.40 (0.95, 2.06)	0.089	0.96 (0.53, 1.71)	0.876
Used an HDSS but never shared any type of syringe	2.80 (1.80, 4.38)	< 0.001	2.25 (1.30, 3.90)	0.004
Used an HDSS, and shared LDSSs	5.60 (3.32, 9.44)	< 0.001	2.85 (1.43, 5.69)	0.003
Used and shared HDSSs	4.83 (2.94, 7.95)	< 0.001	2.21 (1.12, 4.35)	0.022

\* LDSS = low dead -pace syringe

\*\* HDSS = high dead space syringe

**Table 4**  
Bivariate and multiple logistic regression models for HCV among IDUs that deny receptive syringe sharing

	Bivariate logistic regression		Multiple logistic regression	
	Odds ratio (95% confidence interval)	p-value	Adjusted odds ratio (95% confidence interval)	p-value
Age	1.08 (1.06, 1.11)	< 0.001	1.05 (1.01, 1.09)	0.008
Race/ethnicity		0.907		0.179
Non-Hispanic white	Ref	—	Ref	—
African-American	0.97 (0.60, 1.59)	0.927	0.65 (0.34, 1.24)	0.191
Other	1.16 (0.50, 2.71)	0.731	1.38 (0.47, 4.00)	0.558
Male	1.02 (0.65, 1.60)	0.920	0.88 (0.49, 1.59)	0.680
Recruited in Raleigh	0.61 (0.41, 0.92)	0.017	0.63 (0.37, 1.06)	0.079
Homeless	0.68 (0.45, 1.02)	0.063	0.58 (0.34, 0.99)	0.047
Ever in prison	1.37 (0.93, 2.01)	0.114	1.24 (0.74, 2.06)	0.417
Ever in methadone maintenance	3.06 (1.83, 5.10)	< 0.001	2.06 (1.09, 3.88)	0.026
Ever had a sexually transmitted infection	1.30 (0.99, 1.72)	0.063	1.02 (0.61, 1.70)	0.953
Years since first injection		< 0.001		0.001
0–10	Ref	—	—	—
11–20	1.34 (0.78, 2.26)	0.270	1.19 (0.63, 2.25)	0.601
21–30	4.64 (2.65, 8.12)	< 0.001	2.86 (1.34, 6.08)	0.006
31 or more	9.33 (4.70, 18.55)	< 0.001	5.36 (2.01, 14.26)	0.001
Number of injections past 30 days	1.00 (1.00, 1.01)	0.097	1.00 (1.00, 1.01)	0.400
Pharmacy primary source of syringes	1.93 (1.29, 2.90)	0.001	2.11 (1.25, 3.57)	0.005
Indirect sharing/syringe-mediated drug-sharing practices lifetime		0.004		0.254
Never any type of indirect sharing or syringe-mediated drug sharing	Ref	—	—	—
Shared cookers, cottons, or rinse water but never any type of syringe-mediated drug sharing	2.11 (1.05, 4.25)	0.036	2.14 (0.76, 6.03)	0.150
Syringe-mediated drug sharing	2.13 (1.26, 3.61)	0.005	0.75 (0.31, 1.79)	0.515
Ever used an HDSS *	2.42 (1.59, 3.68)	< 0.001	1.29 (0.70, 2.38)	0.420
Indirect sharing/syringe-mediated drug sharing practices lifetime by ever used an HDSS	—	—		0.030
Never used an HDSS use × never any type of indirect sharing or syringe-mediated drug sharing	—	—	Ref	—
HDSS use × shared cookers, cottons, or rinse water but never any type of syringe-mediated drug sharing	—	—	2.52 (0.38, 16.91)	0.342
HDSS use × syringe-mediated drug sharing	—	—	6.42 (1.56, 26.37)	0.010

\* HDSS = high dead-space syringe