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Introduction

Syringes with attached needles (low dead space syringes [LDSS]) retain far less blood following injection than syringes with detachable needles (high dead space syringes [HDSS]). People who inject drugs (PWID) who share needles/syringes may be less likely to acquire Hepatitis C virus (HCV) infection using LDSS, compared with HDSS, but data are limited.

Methods

Utilising drug behaviour and HCV antibody testing data from the UK 2014/2015 Unlinked Anonymous Monitoring Survey of PWID, we calculated the percentage of syringes used in the past month that were LDSS. We investigated which injecting characteristics and demographic factors were associated with 100% LDSS (against 0-99%) usage, and whether 100% LDSS use was associated with antibody HCV-status, after adjusting for confounders.

Result

Of 2,174 participants, 55% always used LDSS, 27% always used HDSS, and 17% used both LDSS and HDSS. PWID that had injected into their groin during the past month were unlikely to use LDSS, adjusted odds ratio (aOR) 0.14 (95% confidence interval 0.11-0.17), compared to those not using the groin. Those injecting crack were less likely to use LDSS than those not, aOR 0.79 (0.63-0.98). Polydrug use was negatively associated with LDSS use, aOR 0.88 (0.79-0.98) per additional drug. LDSS use was associated with lower prevalent HCV among all PWID (aOR 0.77, [0.64-0.93]), which was stronger among recent initiates (aOR 0.53 [0.30-0.94]) than among experienced PWID (aOR 0.81 [0.66-0.99]).

Discussion

People who inject into their groin were less likely to use LDSS. Exclusive LDSS use was associated with lower prevalence of HCV amongst PWID that started injecting recently, suggesting LDSS use is protective against HCV.

Key words

Low dead space syringes, high dead space syringes, safe injecting, injecting drugs, IDU, HCV

Highlights:

- In the UK, people injecting into their groin were less likely to use low deadspace syringes (LDSS)
- Exclusive use of LDSS was associated with lower HCV prevalence among people who inject drugs (PWID)
- This association was stronger among recent initiates than among experienced PWID
- Half of the PWID sampled reported always using LDSS

Introduction

People who inject drugs (PWID) are at risk of blood borne viral (BBV) infections through the sharing of needles, syringes and other injecting equipment(Corson et al., 2013). As a consequence, the prevalence of BBV infections, such as hepatitis C virus (HCV), amongst PWID are high(McLauchlan et al., 2017). The high prevalence in this population means that prevention efforts to reduce the transmission of BBVs among PWID are important. Although evidence is increasing that needle and syringe programmes (NSP) and opiate substitution therapy can decrease the risk of HCV acquisition(Platt et al., 2017; Platt et al., 2016; Turner et al., 2011; World Health Organization, 2012), modelling suggests they are insufficient to reduce HCV to low levels even when there is high coverage(Vickerman et al., 2012), so other prevention or treatment strategies are required to further reduce the burden of disease.

Syringes with attached needles typically have a lower 'dead space', and so retain far less blood following an injection than syringes that have detachable needles(Binka et al., 2015; Grund et al., 1996; Paintsil et al., 2010; Vickerman et al., 2013; Zule et al., 1997), see figure 1. For PWID that share injecting equipment, using low dead space syringes (LDSS) instead of high dead space syringes (HDSS) may lead to a reduced risk of acquiring BBV infections. This is because the volume of blood held in a syringe is an important predictor of the viral load transmitted, as well as virus survival outside of the body(Abdala et al., 1999). The World Health Organization recommends that LDSS are supplied by NSPs to prevent the transmission of BBV(World Health Organization, 2012), although evidence for their prevention benefit is limited(Ambekar and Pawar, 2013; Gyarmathy et al., 2009; Zule and Bobashev, 2009; Zule et al., 2002).

Research into which subgroups of PWID use LDSS and what factors predict LDSS usage has been limited. Awareness of alternatives to HDSS and the inability to successfully access

veins have been discussed as possible barriers to LDSS use in face-to-face interviews with PWID(Kesten et al., 2017). Some research indicates HDSS with longer needles are required for injecting into femoral veins such as those around the groin, and some injectors prefer them because they allow replacement of needles during an injection episode, which is needed if the needle gets blocked or blunt from repeated attempts to find a vein(Zule et al., 2013; Zule et al., 2015).

In this study, we investigated the characteristics of LDSS users amongst PWID and examined whether the type of syringe used was associated with reduced odds of HCV infection in the UK.

Methods

Data

We used data from the 2014 and 2015 Unlinked Anonymous Monitoring Survey (UAM), an annual sero-behavioural survey of PWID recruited from centres providing drug treatment, NSPs and outreach work across England, Wales and Northern Ireland, that has been described in detail previously(Cullen et al., 2015). Those who agreed to participate were asked about their drug use behaviours and demographic information and provided a dried blood spot sample that was tested for HCV antibodies (anti-HCV). The study has ethical approval.

Participants were included if they reported injecting in the past month and had a HCV test result. Those taking part in 2015 who reported taking part previously in 2014 were excluded as repeats. For each participant, we calculated the percentage of syringes used in the past month that were LDSS or HDSS based on self-reported use of syringes with either detachable

or attached needles from the questions "How many individual needles (including ones attached to syringes) did you get from Needle Exchanges during the last month (28 days)?", "How many of these needles were already attached to syringes (barrels)?" these question versions were introduced into the survey in 2014. LDSS with detachable needles were rare in the UK at the time of these surveys as they had not been introduced by NSPs during this period(Abdala et al., 2016). Needles received from NSPs should cover almost all needles received in the UK, as public health funded NSPs are widely available throughout the UK, and over the counter sales of needles are restricted. We excluded participants without information on LDSS use. We used multiple imputation by chained equations to account for missing data in covariates, using five imputed datasets. Stata 14.2 statistical software was used to analyse the data.

Statistical methods

Characteristics of LDSS users

We tabulated demographic information and reported drug use behaviours against the proportion of syringes used that were LDSS in the past 28 days, with this grouped into 0-99%, and 100% LDSS use.

To investigate which subgroups of PWID used LDSS all the time (throughout the last month), we used logistic regression to estimate the unadjusted odds ratio (OR), with 95% confidence intervals (CI), of 100% LDSS (against 0-99%) usage by the following variables: location (with London region as the comparator); age; gender; years since first injection; days injecting past month; type of drug injected in the past month (individual variables for: heroin, methadone, crack, cocaine, speed, ketamine, mephedrone, "other drug"); whether they injected into their groin in the past the month (versus not injecting into their groin); whether

they had been homeless in the past year; whether they had ever received used works from anyone; whether they had shared any injecting equipment (needles/syringes/spoons/filter) during the past month; whether they had ever been in prison; and polydrug use (an integer between 1 and 8, OR per unit increase in types of drug used)

We used multivariable logistic regression with backwards selection of predictors, using an alpha of 0.05, to estimate the adjusted odds ratio (aOR), with 95% CI, for 100% LDSS (against 0-99%) usage, including the variables listed above, except for polydrug use. We did a separate analysis including all variables except the individual drug variables, which were replaced by polydrug use.

We included in the multivariable model variables that were selected in the majority of the backwards stepwise regressions in the imputed datasets. Estimates were aggregated across the imputed datasets using Rubin's rules(Sterne et al., 2009).

LDSS usage and HCV infection

We used logistic regression to estimate the unadjusted and adjusted association of 100% LDSS use, compared to any HDSS use, with prevalent anti-HCV. Variables assessed for inclusion in the adjusted model were groin injecting, injecting crack in the past month, injecting heroin past month, injecting "other drugs" past month, years since first injection, any equipment or syringe sharing in the past month, injection frequency (number of days injected past month multiplied by the frequency of injecting on the last day they injected), ever been to prison, and homelessness in the previous year.

As injecting in the groin requires longer needles that are usually HDSS(Kesten et al., 2017), groin injecting and HDSS usage were highly correlated, with both potentially being risk factors for HCV infection as groin injecting is associated with other risky behaviours(Rhodes et al., 2006). We did not include groin injecting as a confounder in the multivariable model because of this collinearity and the possibility that it is on the causal pathway. We repeated the analysis adjusting for polydrug use, instead of adjusting for crack, heroin, and "other" drug use.

Many of the prevalent HCV infections will have occurred in the past, potentially many years ago; it is therefore likely that some behaviours measured by the survey will not be representative of the behaviours at the time of infection. We therefore fitted a model that included an interaction term between LDSS use and whether a PWID recently started injecting – defined as less than 3 years ago. In a sensitivity analysis, we varied the threshold for the definition of recently initiating injecting from 2 to 10 years to examine how recency of initiation influenced the association between LDSS usage and HCV prevalence.

Results

Demographics and injecting characteristics

Of 3,083 surveyed individuals who had injected in the previous month, 909 (28%) were excluded as they had missing information on LDSS use. Compared to included PWID, those excluded were similar in age, a similar proportion had ever been imprisoned, and a slightly higher proportion were females. Of those 2,174 participants with information on LDSS use over the past month, 55% always used LDSS, 17% used both LDSS and HDSS, and 27% always used HDSS (table 1). Almost all (98%) participants that injected in the previous

month responded to the question about injecting into the groin, with 32% reporting they had done so.

Amongst the PWID analysed, 90% had injected heroin in the past month, and of the 10% who had not injected heroin, 72% had injected amphetamine (speed). The median age was 37 years, 24% were female, and 95% were born in the UK. The mean number of days injected in the previous month was 17 (median 16) and the mean time since first injection was 15 years (median 15). Just over half (55%, 1,191) tested positive for HCV antibodies.

Predictors of LDSS usage

Table 1 shows cross tabulations of LDSS usage in last month by demographic and injecting characteristics. LDSS usage varied by geographical region, table 2. The highest proportion of participants that only used LDSS in the past month was from the West Midlands (68%), with London second highest at 66%, and the East Midlands the lowest at 45%. Exclusive LDSS use was reported by PWID regardless of years since first injection, although it was more common in those who had been injecting for fewer years (supplementary figure 1[λ]). Otherwise, HDSS and LDSS users have similar characteristics except for previous imprisonment, crack injecting, and injecting into the groin. Two-thirds (66%) of PWID that always used LDSS had ever been to prison, compared to 77% of PWID that used HDSS. Injecting crack during the last month was more common in HDSS users, compared with those who always used LDSS (47% versus 39%). Injecting into the groin during the last month was strongly associated with HDSS use (64% and 20% injected into the groin amongst those who had used HDSS or only used LDSS, respectively).

Predictors of 100% LDSS usage included geographic region, type of drug injected and injection site (table 3). Compared to not injecting that drug, injecting crack was predictive of not using LDSS, (aOR 0.79 [0.63-0.98]), as was injecting "other drugs" (aOR 0.63 [0.42-

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0.95]), whereas injecting heroin was predictive of using LDSS (aOR 1.47 [1.04-2.08]). Those injecting into the groin were very unlikely to use LDSS, aOR 0.14 (0.11-0.17), compared to those not injecting into the groin. Selection of variables was consistent over the imputed datasets (supplementary table 1[λ]). In the analysis including polydrug use instead of the individual drug variables, we found that polydrug use was negatively associated with 100% LDSS use, with an aOR of 0.88 (0.79-0.98) per each additional type of drug injected.

LDSS usage and HCV infection

Overall, the HCV prevalence amongst PWID included in the analyses was 55% (53%-57%), with it being lower amongst those only using LDSS (50% [47%-53%]) compared to those using HDSS (61% [58%-64%]). The proportion with anti-HCV also increased with years since first injection and was consistently lower amongst PWID using LDSS across all injecting durations (figure 2).

Compared to any HDSS use, exclusive LDSS use during the last month was associated with lower odds of having anti-HCV (table 4, OR 0.64 [0.54-0.76]). In the model adjusted for confounders, years since first injection, sharing injecting equipment, injecting crack, and having been to prison were all associated with increased odds of having anti-HCV (supplementary table 2[λ]), whereas exclusive LDSS use was associated with lower odds of having anti-HCV [aOR 0.77 (0.64-0.93)] when compared with any HDSS use, table 4. Polydrug use was associated with increased odds of having HCV (unadjusted OR 1.46 (1.31-1.62) and adjusted OR 1.38 (1.23-1.55) per additional type of drug. However, the aOR for 100% LDSS use (vs 0-99%) on HCV remained unchanged.

Among PWID that had reported starting injecting more recently, exclusive LDSS use was associated strongly with lower odds of prevalent anti-HCV. Supplementary figure 2[λ] shows the magnitude of the association was greater when the duration threshold used to define

recent initiation was shorter. Amongst those who had injected for less than 3 years, the OR of anti-HCV was 0.46 (0.26, 0.80) for exclusive LDSS use compared to any HDSS use (table 5a), which attenuated to 0.53 (0.30, 0.95) after adjusting for other variables. In the model adjusted for confounders, years since first injection, sharing injecting equipment, injecting crack, and having been to prison were all associated with increased odds of anti-HCV infection (supplementary table 3[λ]). Although groin injecting was strongly associated with anti-HCV prevalence (OR 2.35 [1.96-2.81]), the effect of LDSS on anti-HCV prevalence was independent of this association in those who started injecting recently and were therefore less likely to inject in the groin. Table 5b also presents the aOR for exclusive LDSS use for PWID that had not started injecting recently (>3 years), 0.81 (0.66, 0.99), compared with those who had started injecting more recently and used HDSS. This shows that the association between exclusive LDSS use and lower odds of anti-HCV seen amongst all PWID is stronger among those who had started injecting more recently.

Discussion

Main findings

Among all PWID, 100% LDSS use during the last month was associated with reduced risk of HCV infection, with this association being stronger amongst recent initiates (injecting less than 3 years). During this period recent behaviours are probably more representative of the behaviours when infection occurred. Half of the PWID sampled reported always using LDSS and a quarter always used HDSS, which was more common among those injecting into their groin or injecting crack or polydrug users. The association with groin injecting is probably related to larger needles being needed when injecting into the femoral vein. Patterns of LDSS use also varied by geographic region, which may reflect differences in LDSS availability or other factors such as what drugs are injected or local preferences.

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When considering the association between LDSS and HCV infection, it is important to note the relationship between these variables and groin injecting. Groin injecting may be a more robust marker of HDSS usage than using questions on the type of syringe use because the latter was less frequently recorded – 98% of participants that injected in the past month answered the groin injecting question, but only 71% answered both questions used to derive the LDSS variable. Groin injecting, due to the preferred size of the needle for this injection site, was strongly correlated with HDSS use, as also found by other studies(Kesten et al., 2017). However, some research suggests that people who inject into the groin also engage in more risky injection practices that could lead to HCV infection(Rhodes et al., 2006). As people in our study who inject into the groin were the main users of HDSS needles and were long-term injectors, we only found an independent effect of LDSS usage on HCV infection when analyses were stratified by recency of initiating injecting.

Comparisons with other literature

To our knowledge this is the first quantitative study measuring LDSS use in the UK. However, comparisons with studies from other settings are restricted due to the variety of questions used to capture information about syringe use. Whilst we found that 55% of UK PWID were currently only using LDSS, studies from Texas, Hungary and Tajikistan found much higher levels of LDSS use, although these studies did not necessarily capture behaviours within the past month(Gyarmathy et al., 2009; Zule et al., 2002; Zule et al., 2015). Elsewhere, other studies from North Carolina, USA, and Tijuana, Mexico, found about 40% of PWID had ever used HDSS(Rafful et al., 2015; Zule and Bobashev, 2009). The variation in findings is unsurprising given the geographic diversity of these studies, although they do suggest that PWID in the UK may have higher use of HDSS than other settings.

Regarding reasons for why LDSS or HDSS are used, a recent qualitative study from Bristol, UK, found an important motivation behind syringe choice was to inject successfully, with changes in syringe use only being considered when problems were encountered(Kesten et al., 2017). We did not have information on why individuals used HDSS or LDSS but were able to examine associations between drug use behaviours and what type of syringe was used. The study in Texas found that LDSS use varied by ethnicity – a variable not recorded in our data, and HDSS increased with years since first injection, which we also found(Zule et al., 2002). In the study from North Carolina, 62% of PWID reporting HDSS use said they did so because they were easier to obtain(Zule and Bobashev, 2009). The study in Tijuana found that HDSS use was mostly because no other syringe type was available, and that it was associated with cocaine use and having been stopped or arrested by police(Rafful et al., 2015). Data from North Carolina, USA, and Russia showed that HDSS use was associated with the use of nonmedical prescription opioids(Zule and Bobashev, 2009; Zule et al., 2016), similar to our finding that LDSS use varies according to the drug injected. Lastly, the study from Tajikistan found that choice of needle length was influenced by the depth of the vein being used, so HDSS were sometimes preferred as the user could select the needle length(Zule et al., 2015). This supports our study finding that HDSS use was preferred amongst those injecting into the groin.

There has been limited research into whether the odds of exposure to HCV infection or other blood borne viruses is related to the type of syringe used by PWID. The Texan study found the proportion of PWID with HIV was higher in those that had ever used HDSS(Zule et al., 2002). Similarly, the North Carolina study found increased HIV and HCV prevalence with increased HDSS use(Zule and Bobashev, 2009), whereas the study from Hungary did not find an association with HCV prevalence(Gyarmathy et al., 2009). Our data adds to these studies, with our analyses adding more rigour by controlling for other determinants of HCV infection.

There are no studies sufficiently powered to estimate the effect of LDSS usage on incident HCV or HIV infection. The dataset used in this study test for biological markers of recent HCV infection(Cullen et al., 2015), but due to issues with power resulting from incident HCV being comparatively rare we were unable to analyse them.

Strengths and limitations

Strengths of our study include the relatively large and geographically diverse sample, which is likely to be a representative subsample of UK PWID. The wide availability of the NSPs in the UK, combined with the restriction on over the counter sales means that NSP provided needles (those considered in this study) should account for the vast majority of needles received in the UK. Another strength of the paper was the availability of variables covering behaviours over the last month, rather than over a lifetime, meaning they are more directly relevant to current practises. However, due to the nature of the questions used to determine LDSS use we were only able to include those that had injected in the past month and who had recently obtained equipment directly from an NSP, so excluding past and less frequent injectors and those not in contact with NSPs. We were also only able to examine injecting practices in the past month and were unable to determine how current practices related to behaviours when they started injecting. We were also unable to determine when they became infected with HCV, which could have been many years ago. Recall bias and social desirability considerations may have also impacted on our result, and there were missing data for many variables, although we used multiple imputation to account for these missing values. Finally, our study is observational and therefore unmeasured confounding may have affected our results.

Implications

Our study found a negative association between LDSS use and HCV infection among PWID. This possible protective association was particularly strong among those who had initiated injecting recently. For determining whether LDSS use reduces the chance of HCV infection it is crucial to understand the interaction and effect of groin injecting. There is no doubt that groin injecting and HDSS use are highly correlated, but we do not know if groin injecting heightens the odds of HCV infection amongst those who use HDSS, or alternatively whether groin injecting was a more reliable marker of HDSS use in our survey. Although it is also possible that HDSS users may in general have higher odds of HCV infection, with certain high-risk markers of HCV (prison and crack injecting) being more prevalent amongst HDSS users than LDSS users, it is known that HDSS retain more blood following an injecting episode(Binka et al., 2015) and therefore transmit a higher viral load when shared (Abdala et al., 1999). This means that using LDSS instead of HDSS is likely to lead to a reduction in risk of HCV transmission among PWID that share equipment.

World Health Organization guidelines on prevention of hepatitis among PWID recommend making LDSS available to reduce blood borne infections(World Health Organization, 2012), despite there currently being limited direct evidence to support this. Although our study supports these guidelines by suggesting LDSS use may be associated with lower odds of infection, further research is still needed to obtain stronger evidence on this effect. This limitation in the evidence base has no doubt slowed down the expansion of LDSS provision, with the availability and use of these syringes varying by region(Ibragimov and Latypov, 2012). It is encouraging to note that nearly half of our sample used LDSS every time they injected in the past month, although over a quarter did not use LDSS. Our study sheds further light on who does and does not use LDSS; LDSS use is inversely associated with injecting behaviours that are considered more chaotic such as crack injecting, polydrug use, and groin injecting(Tweed et al., 2018). The study adds to the evidence that those injecting into deep

lying veins, the groin in our study, are a distinct subset of PWID with specific syringe needs to enable injection into such sites(Kesten et al., 2017). As previous studies have reported injecting into the groin is often considered a last resort once the peripheral veins are no longer useable(Hope et al., 2015), resources and information about safer injection practices and maintaining better vein health should be used to reduce the extent of injection into the groin, and other deep and/or central veins.

Our study also provides crucial information for interventions aiming to increase the use of LDSS amongst PWID, a few of which have recently been initiated(Huong et al., 2015; Oramasionwu et al., 2015). LDSS use is highly related to the type of drug used and the body site injected into; so to operationalise the World Health Organization guidelines we need needles that meet the needs of all PWID while also minimising their dead space. Detachable syringes and needles with lower dead space have been developed and are now being distributed in some settings. However, although they are an improvement, they still have greater dead space than LDSS, resulting in longer survival of HCV within the syringe and greater transfer of virus after syringe sharing(Abdala et al., 2016). It is important that further syringe development occurs to minimise the dead space associated with these syringes while still meeting their need amongst some PWID.

[λ]Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and entering doi: ... 18

Figure 1: Illustrations of the dead space in low and high dead space syringes (artwork licensed by Creative Commons). Reproduced with permission from William Zule.

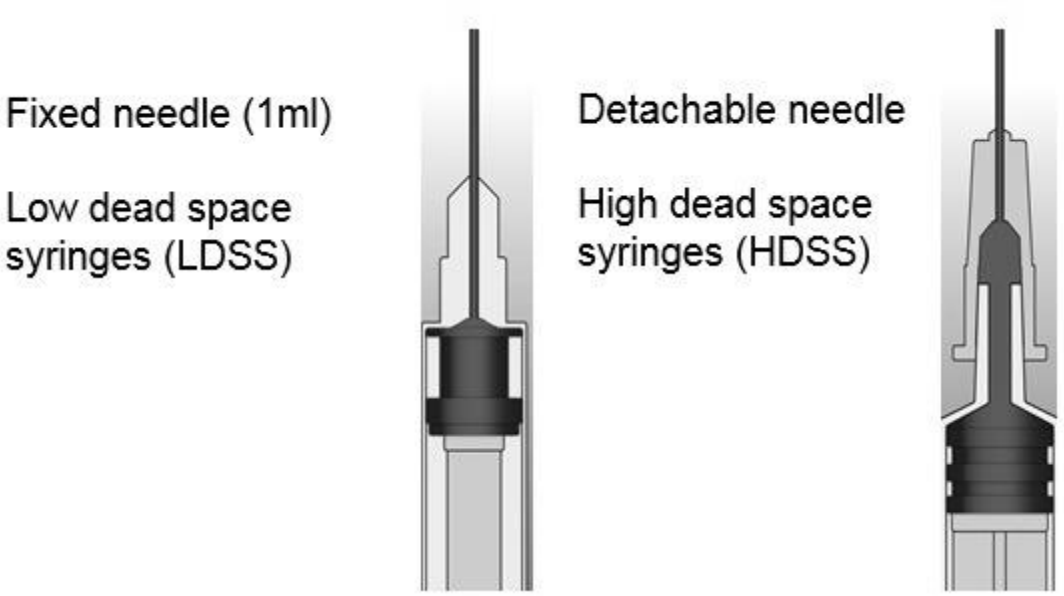
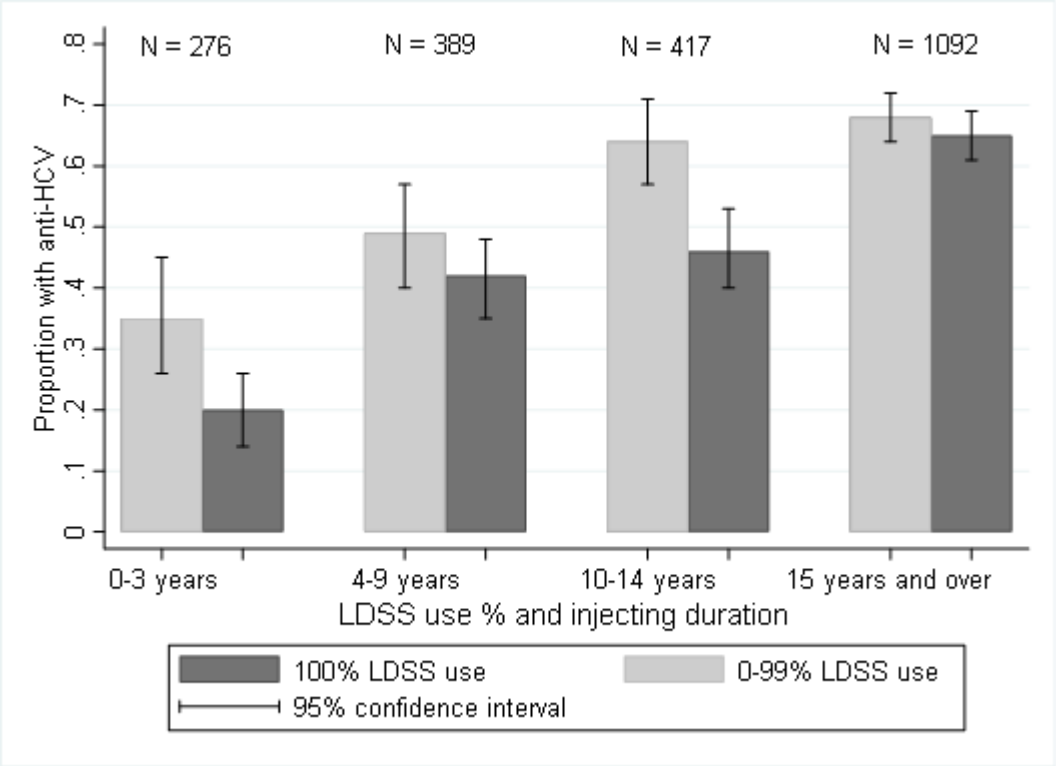


Figure 2: Proportion of PWID with anti-HCV, stratified by number of years since first injection and LDSS use percentage



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Tables

Tables 1: The demographics and injecting characteristics of PWID for each LDSS use category. Results were weighted so N are unavailable.

Variable	0-99% LDSS use	100% LDSS use	Total
Number (%)	**969 (45%)**	**1,205 (55%)**	**2,174 (100%)**
Mean (95% confidence interval)			
Age (years)	38 (37, 38)	37 (36, 37)	37 (37, 37)
Days injecting †	17 (17, 18)	16 (16, 17)	17 (16, 17)
Years since first injection	16 (15, 16)	14 (14, 15)	15 (14, 15)
Number of types of drug injected	1.9 (1.8, 1.9)	1.7 (1.7, 1.8)	1.8 (1.8, 1.8)
Proportion (95% confidence interval)			
Women	23% (21%, 26%)	24% (21%, 26%)	24% (22%, 25%)
Initiated injecting in the past 3 years	10% (8%, 12%)	15% (13%, 17%)	13% (11%, 14%)
Ever been in prison	74% (71%, 77%)	66% (63%, 69%)	70% (68%, 72%)
Homeless in past year	19% (16%, 21%)	19% (16%, 21%)	19% (17%, 20%)
Ever injected with received needles & syringes	36% (33%, 39%)	36% (34%, 39%)	36% (34%, 38%)
Shared equipment †	37% (34%, 40%)	37% (34%, 40%)	37% (35%, 39%)
Injected into groin †	64% (61%, 67%)	20% (18%, 23%)	40% (38%, 42%)
Injected with cleaned works†	29% (26%, 32%)	29% (26%, 31%)	29% (27%, 31%)

Injected heroin †	90% (88%, 92%)	91% (89%, 93%)	90% (89%, 92%)
Injected methadone †	2% (1%, 3%)	1% (1%, 2%)	2% (1%, 2%)
Injected crack †	49% (46%, 52%)	39% (36%, 42%)	43% (41%, 46%)
Injected cocaine †	9% (7%, 11%)	8% (6%, 9%)	8% (7%, 10%)
Injected speed †	22% (20%, 25%)	21% (18%, 23%)	21% (20%, 23%)
Injected ketamine †	2% (1%, 3%)	2% (1%, 3%)	2% (1%, 3%)
Injected mephedrone †	7% (5%, 8%)	5% (4%, 6%)	6% (5%, 7%)
Injected other drug †	7% (5%, 8%)	6% (4%, 7%)	6% (5%, 7%)

† Past month. Missing data was imputed using multiple imputation.

Table 2: The percentage of PWID within each LDSS use category for different geographic locations. Results were weighted so N are unavailable.

Variable	0-99% LDSS use	100% LDSS use	Total
Number (%)	**969 (45%)**	**1,205 (55%)**	**2,174 (100%)**
Location	**% of LDSS use category across geographic location**		
Total	45%	55%	100%
London	34%	66%	8%
East England	51%	49%	7%
South East	41%	59%	10%
South West	44%	56%	10%
West Midlands	32%	68%	8%
North West	53%	47%	12%
Yorkshire & Humber	52%	48%	10%
East Midlands	55%	45%	13%
North East	39%	61%	8%
Wales	39%	61%	12%
Northern Ireland	49%	51%	2%

Table 3: Unadjusted and mutually adjusted odds ratios (OR) with 95% confidence intervals of 100% LDSS use (against 0-99% LDSS use).

	Odds Ratios (95% confidence intervals) of 100% LDSS use					
Variable	**Unadjusted OR**	**P/wald-value**	**Adjusted OR***	**P/wald-value**	**Adjusted OR****	**P/wald-value**
Injected heroin †	1.10 (0.83, 1.47)	0.507	1.47 (1.04, 2.08)	0.028	NA	NA
Injected crack †	0.67 (0.57, 0.80)	<0.001	0.79 (0.63, 0.98)	0.032	NA	NA
Injected other drug †	0.80 (0.56, 1.14)	0.226	0.63 (0.42, 0.95)	0.028	NA	NA
Injected into groin †	0.14 (0.12, 0.17)	<0.001	0.14 (0.11, 0.17)	<0.001	0.14 (0.12, 0.17)	<0.001
No. of types of drug injected (per drug) †	0.81 (0.74, 0.90)	<0.001	NA	NA	0.88 (0.79, 0.98)	0.024
London	1		1		1	
East England	0.49 (0.31, 0.77)	0.002	0.50 (0.30, 0.83)	0.007	0.51 (0.31, 0.84)	0.008
South East	0.73 (0.48, 1.10)	0.131	0.95 (0.60, 1.50)	0.823	0.94 (0.60, 1.50)	0.806
South West	0.63 (0.42, 0.96)	0.030	0.85 (0.54, 1.35)	0.497	0.81 (0.51, 1.29)	0.374
West Midlands	1.05 (0.67, 1.64)	0.821	1.16 (0.70, 1.91)	0.565	1.17 (0.71, 1.92)	0.538
North West	0.45 (0.30, 0.67)	<0.001	0.60 (0.38, 0.94)	0.024	0.59 (0.38, 0.92)	0.020
Yorkshire	0.47 (0.31, 0.71)	<0.001	0.64 (0.40, 1.02)	0.059	0.64 (0.41, 1.01)	0.056
East Midlands	0.42 (0.28, 0.62)	<0.001	0.48 (0.31, 0.75)	0.001	0.48 (0.31, 0.74)	0.001
North East	0.78 (0.51, 1.21)	0.268	0.89 (0.54, 1.46)	0.637	0.93 (0.57, 1.51)	0.761
Wales	0.80 (0.54, 1.20)	0.289	1.01 (0.64, 1.60)	0.974	1.03 (0.66, 1.60)	0.913
Northern Ireland	0.53 (0.27, 1.02)	0.058	0.44 (0.21, 0.93)	0.031	0.45 (0.22, 0.92)	0.030
Days injecting†	0.99 (0.98, 1.00)	0.018	NA			
Age (years)	0.99 (0.98, 1.00)	0.009	NA			
Years since first injection	0.98 (0.97, 0.99)	<0.001	NA			
Injected methadone †	0.68 (0.36, 1.28)	0.234	NA			
Injected cocaine †	0.80 (0.59, 1.09)	0.152	NA			
Injected speed †	0.90 (0.73, 1.10)	0.298	NA			

Injected ketamine †	1.06 (0.58, 1.94)	0.853	NA
Injected mephedrone †	0.72 (0.49, 1.05)	0.084	NA
Homeless last year	1.00 (0.80, 1.24)	0.989	NA
Female	1.01 (0.83, 1.24)	0.924	NA
Ever injected with received needles & syringes	1.00 (0.84, 1.20)	0.966	NA
Reported sharing injecting equipment †	1.00 (0.84, 1.19)	0.993	NA
Ever imprisoned	0.69 (0.57, 0.83)	<0.001	NA

† Past month

*The adjusted OR were adjusted for variables selected in the multivariable model which did not include number of types of drug injected.

**The adjusted OR for number of types of drug was adjusted for geographical location and groin injecting and not for heroin, crack, or other drug.

Table 4: Odds ratios (OR) of being anti-HCV positive (i) unadjusted, (ii) adjusted – with the percentage of the sample in each category, and the percentage of each group with HCV infection. N=2,174.

Variable	%	% HCV +ve	Unadjusted OR	Adjusted OR
0-99% LDSS use	45%	61%	1	1
100% LDSS use	**55%**	**50%**	**0.64 (0.54, 0.76)**	**0.77 (0.64, 0.93)**

Adjusted for the following variables: Injections (every 10) per month, shared equipment last month, years since first injection, injecting crack, injecting heroin, injecting "other drug", ever been in prison, and homeless in the last year.

Table 5: Odds ratios (OR) of being anti-HCV positive, including an interaction term between LDSS use and having started injecting during the last 3 years. Table 5a shows the interaction using 0-99% LDSS users who are recent starters as the comparator group, whilst for Table 5b the comparator is 0-99% LDSS users who are non-recent starters.

(a) Variable	%	% HCV +ve	Unadjusted OR	Adjusted OR
0-99% LDSS use & recent starter	5%	35%	1	1
100% LDSS use & recent starter	**8%**	**20%**	**0.46 (0.26, 0.80)**	**0.53 (0.30, 0.94)**

(b) Variable	%	% HCV +ve	Unadjusted OR	Adjusted OR
0-99% LDSS use & non-recent starter	40%	64%	1	1
100% LDSS use & non-recent starter	**47%**	**55%**	**0.70 (0.58, 0.85)**	**0.81 (0.66, 0.99)**

Adjusted for the following variables: Injections (every 10) per month, shared equipment past month, years since first injection, injecting crack, injecting heroin, injecting "other drug", and ever been in prison, and homeless in the past year. N=2,174.

Supplementary table 1: The adjusted Odds Ratios with 95% confidence intervals of 100% LDSS use (against 0-99% LDSS use) produced from a logistic regression model using backwards stepwise selection on each of the five imputed datasets.

	Backwards Stepwise Logistic Regression, Adjusted Odds Ratios (95% Confidence Interval)				
Variable	**Imputed set 1**	**Imputed set 2**	**Imputed set 3**	**Imputed set 4**	**Imputed set 5**
Location					
London	1	1	1	1	1
East England	0.51 (0.31, 0.85)	0.50 (0.31, 0.83)	0.51 (0.31, 0.85)	0.52 (0.32, 0.86)	0.51 (0.31, 0.84)
South East	0.96 (0.61, 1.52)	0.93 (0.59, 1.48)	0.95 (0.60, 1.51)	0.97 (0.61, 1.54)	0.94 (0.59, 1.49)
South West	0.84 (0.53, 1.34)	0.86 (0.54, 1.37)	0.87 (0.55, 1.38)	0.89 (0.56, 1.41)	0.85 (0.54, 1.36)
West Midlands	1.14 (0.69, 1.87)	1.14 (0.69, 1.87)	1.14 (0.69, 1.88)	1.19 (0.72, 1.98)	1.13 (0.69, 1.87)
North West	0.60 (0.39, 0.94)	0.61 (0.39, 0.95)	0.59 (0.38, 0.93)	0.63 (0.40, 0.98)	0.60 (0.38, 0.94)
Yorkshire	0.62 (0.39, 0.98)	0.62 (0.39, 0.99)	0.62 (0.39, 0.99)	0.65 (0.41, 1.04)	0.62 (0.39, 0.99)
East Midlands	0.46 (0.30, 0.72)	0.47 (0.30, 0.73)	0.50 (0.30, 0.73)	0.49 (0.31, 0.77)	0.46 (0.30, 0.72)
North East	0.86 (0.52, 1.42)	0.85 (0.52, 1.41)	0.87 (0.52, 1.43)	0.93 (0.56, 1.55)	0.86 (0.52, 1.42)
Wales	1.00 (0.63, 1.58)	1.00 (0.63, 1.58)	1.01 (0.64, 1.60)	1.05 (0.66, 1.68)	1.00 (0.63, 1.59)
Northern Ireland	0.41 (0.20, 0.87)	0.42 (0.20, 0.88)	0.42 (0.20, 0.89)	0.43 (0.20, 0.90)	0.41 (0.20, 0.87)
Previous study participation	1.25 (0.98, 1.60)	1.20 (0.94, 1.53)	1.26 (0.99, 1.61)	1.22 (0.96, 1.56)	1.21 (0.95, 1.54)
Born in the UK	Not Included	Not Included	Not included	0.73 (0.47, 1.15)	Not Included
Groin injector	0.14 (0.11, 0.17)	0.14 (0.11, 0.17)	0.14 (0.11, 0.17)	0.14 (0.11, 0.17)	0.14 (0.11, 0.17)
Injected crack	0.79 (0.63, 0.98)	0.77 (0.62, 0.96)	0.80 (0.64, 0.99)	0.79 (0.64, 0.98)	0.78 (0.63, 0.98)
Injected heroin	1.46 (1.04, 2.05)	1.44 (1.03, 2.02)	1.53 (1.09, 2.15)	1.45 (1.04, 2.03)	1.54 (1.10, 2.17)

Injected other	0.64 (0.43, 0.96)	0.63 (0.42, 0.88)	0.63 (0.42, 0.94)	0.63 (0.42, 0.95)	0.66 (0.44, 0.98)

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Supplementary table 2: Odds ratios (OR) of being anti-HCV positive (against negative) (i) unadjusted, (ii) adjusted. N=2,174.

Variable	Unadjusted	Adjusted
0-99% LDSS use	1	1
100% LDSS use	**0.64 (0.54, 0.76)**	**0.77 (0.64, 0.93)**
Injections (every 10) per month	1.11 (0.92, 1.33)	1.10 (0.90, 1.35)
Shared equipment last month	1.22 (1.01, 1.46)	1.28 (1.05, 1.56)
Years since first injection	1.08 (1.07, 1.09)	1.07 (1.06, 1.08)
Injecting crack	2.58 (2.15, 3.09)	2.23 (1.83, 2.71)
Injecting heroin	1.67 (1.24, 2.24)	1.20 (0.86, 1.67)
Injecting "other drug"	0.77 (0.54, 1.11)	0.78 (0.53, 1.17)
Injecting into groin	2.35 (1.96, 2.81)	NA
Ever been in prison	2.83 (2.34, 3.42)	2.11 (1.72, 2.59)
Homeless in last year	1.18 (0.95, 1.47)	1.23 (0.97, 1.57)

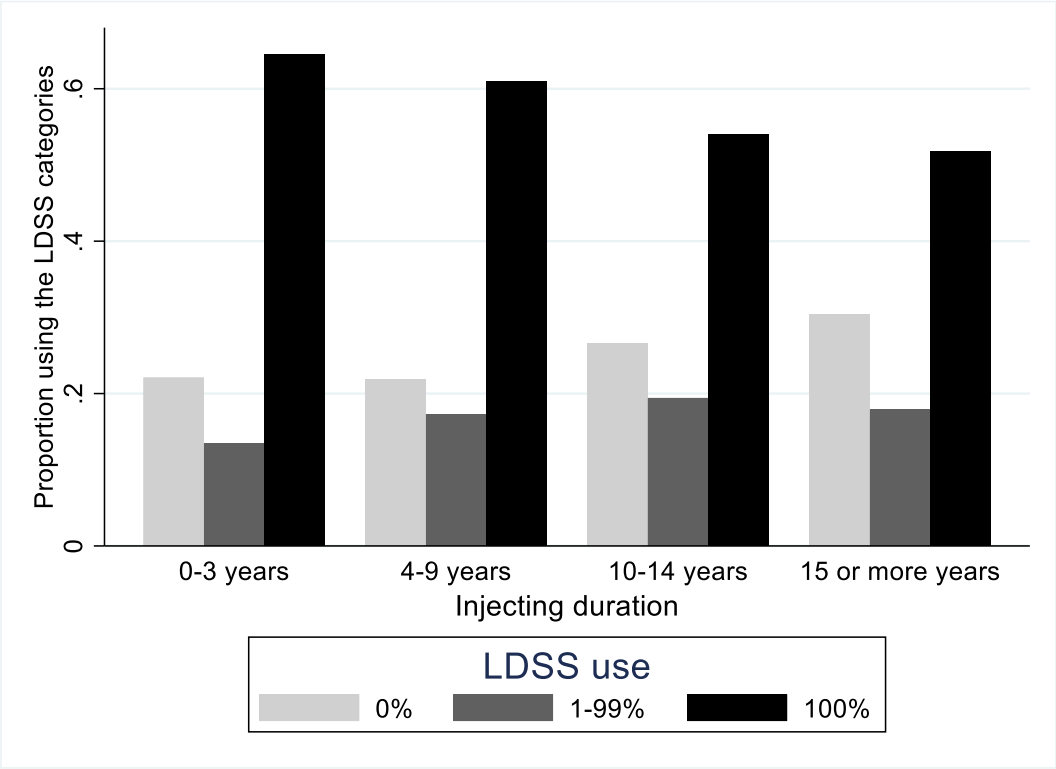
Groin injecting was not included in the adjusted model as syringe type was on the causal pathway between groin injecting and HCV.

Supplementary table 3: Odds ratios (OR) of being anti-HCV positive (against negative), including an interaction term between LDSS use and having started injecting during the last 3 years (i) unadjusted, (ii) adjusted. N=2,174.

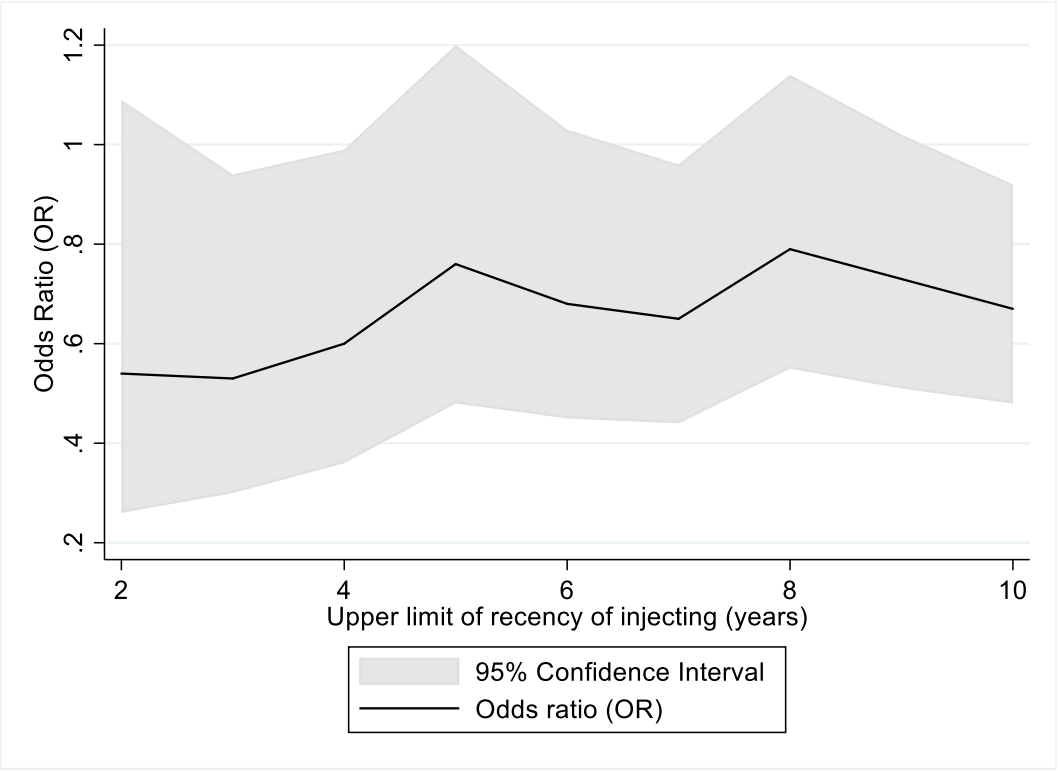
Variable	Unadjusted	Adjusted
0-99% LDSS use & recent starter	1	1
100% LDSS use & recent starter	**0.46 (0.26, 0.80)**	**0.53 (0.30, 0.94)**
0-99% LDSS use & non-recent starter	3.23 (2.08, 5.02)	1.23 (0.75, 2.04)
100% LDSS use & non-recent starter	2.27 (1.47, 3.51)	1.00 (0.61, 1.63)
Injections (every 10) per month	1.11 (0.92, 1.33)	1.10 (0.90, 1.35)
Shared equipment last month	1.22 (1.01, 1.46)	1.29 (1.06, 1.58)
Years since first injection	1.08 (1.07, 1.09)	1.06 (1.05, 1.08)
Injecting crack	2.58 (2.15, 3.09)	2.26 (1.85, 2.76)
Injecting heroin	1.67 (1.24, 2.24)	1.17 (0.84, 1.64)
Injecting "other drug"	0.77 (0.54, 1.11)	0.78 (0.52, 1.17)
Injecting into groin	2.35 (1.96, 2.81)	NA
Ever been in prison	2.83 (2.34, 3.42)	2.07 (1.68, 2.54)
Homeless in last year	1.18 (0.95, 1.47)	1.24 (0.97, 1.58)

Groin injecting was not included in the adjusted model as syringe type was on the causal pathway between groin injecting and HCV.

Supplementary figure 1: The proportion of PWID in each LDSS use category, stratified by number of years since first injection.



Supplementary figure 2: The adjusted Odds Ratios of anti-HCV positivity, for 100% LDSS use (versus 0%-99% LDSS use) amongst PWID that have recently started injecting, varied by the threshold (number of years) used to define recent initiation of injecting. This figure shows the bolded result in the adjusted column of supplementary table 3, using different definitions of having recently started injecting.



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