Aspinall E., Weir, A., Sacks-Davis, R., Spelman T., Grebely J., Higgs P., Hutchinson S., Hellard M. [ACCEPTED VERSION]. Does informing people who inject drugs of their hepatitis C status influence their injecting behavior? Analysis of the Networks II study, *International Journal of Drug Policy,*

ABSTRACT

Background: People who inject drugs (PWID) are at risk of hepatitis C virus (HCV). It is plausible that PWID who receive a diagnosis of HCV will reduce their injecting risk out of concern for their injecting partners, although evidence for this is currently limited. The aim of this study was to investigate whether informing PWID of their HCV diagnosis was associated with a change in injecting behaviour.
Methods: Prospective, longitudinal study of PWID recruited from street drug markets across Melbourne, Australia. Interviews and HCV testing were conducted at 3-monthly intervals. The association between receiving a diagnosis of HCV and (i) injecting frequency and (ii) injecting equipment borrowing, was examined using generalized estimating equations (GEE) analysis.
Results: Thirty-five individuals received a diagnosis of HCV during the study period. Receiving a diagnosis of HCV was associated with a decrease of 0.35 injections per month ($p = 0.046$) but there was no change in injecting equipment borrowing ($p = 0.750$).
Conclusions: A small reduction in injecting frequency was observed in PWID who received a diagnosis of HCV. This finding should be investigated further in larger studies examining a wider range of injecting risk behaviours.

Introduction

Hepatitis C virus (HCV) is a significant cause of morbidity and mortality amongst people who inject drugs (PWID) (Grebely & Dore, 2011). Screening PWID for HCV infection has been rec- ommended as a means of supporting infected individuals into appropriate care pathways, and providing advice on safer injecting practice to reduce HCV transmission (WHO, 2011). It seems plausi- ble that PWID who are diagnosed with HCV, and receive counselling on the risks of HCV transmission, will subsequently reduce their injecting risk behaviour in order to decrease their chance of trans- mitting HCV to others.

Few studies have examined the impact of HCV diagnosis on injecting behaviour: Tsui et al. (2009) found no change in inject- ing drug use, equipment sharing, or equipment lending amongst a cohort of young PWID followed over a 12-month period, and Ompad, Fuller, Vlahvov, Thomas, and Strathdee (2002) reported no change in the sharing of needles, syringes or other injection para- phernalia six months after receiving a diagnosis of HCV. Aitken, Kerger, and Crofts (2002) found an increase in the use of new needles and syringes three months following HCV testing and counselling, but there was no difference between people receiv- ing positive or negative HCV results. However, these studies were limited by relatively short periods of follow-up.

The Networks II study followed a cohort of PWID over a period of five years, with the aim of understanding the transmission of blood borne viruses (BBV) amongst a social network of PWID. The aim of this study was to determine whether, in this cohort of PWID, informing an individual of their HCV diagnosis was associated with a change in injecting behaviour, compared to injecting behaviour prior to HCV diagnosis.

Methods

Participants

PWID who reported that they had injected in the previous six months were recruited from three major street drug markets located across Melbourne. PWID aged 16–25 years, or who were not infected with HCV, were preferentially recruited. Participation was voluntary, and informed consent in writing was obtained

from each participant. The Victorian Department of Human Services Human Research Ethics Committee approved the study.

Data collection

Participants were recruited between July 2005 and 2007, with follow-up continuing until December 2010. At baseline and three-monthly intervals, participants underwent venepuncture and face-to-face interviews with outreach workers trained in pre and post-test discussions for blood borne viruses (BBVs). At each visit, participants were asked (i) how often they had injected in the previous month and (ii) the number of times injected in the previ- ous three months using a needle and syringe that had already been used by someone else (hereafter referred to as 'borrowing').

Blood samples were screened for anti-HCV antibody (anti-HCV) by a third-generation enzyme immunoassay (Abbott Laborato- ries, Chicago, IL) and positive specimens were confirmed using the Murex anti-HCV antibody test, version 4.0 (Murex Biotech, Kyalami, South Africa). Irrespective of anti-HCV status, all sam- ples were tested for HCV RNA using COBAS AMPLICOR HCV test version 2.0 (Roche Molecular Systems, Branchburg, NJ). Individ- uals testing negative for anti-HCV were tested for anti-HCV and HCV RNA at subsequent visits. Individuals testing positive for anti- HCV were retested for HCV RNA, but not antibody, at subsequent visits. Participant interviews lasted on average 30–40 min (includ- ing venepuncture), and participants were reimbursed AU$25 cash for each interview attended.

Pre and post-test discussion

The pre-test discussion was provided by trained interviewers and has been described in detail elsewhere (Winter et al., 2008). The aims were to ensure the participant was aware of the pros and cons of being tested, to investigate the support required in the event of a positive test, and to provide information on the transmission and prevention of HCV.

Efforts to contact participants were made as soon as test results became available, which was normally within two to four weeks of testing. In a small number of cases, participants could not imme- diately be contacted, and test results were provided more than four weeks after the test date. Participants receiving a positive HCV RNA test for the first time were provided with information about the interpretation of the test results, strategies for minimiz- ing the risk of HCV transmission, and appropriate steps for further assessment of their HCV by a healthcare professional. Printed HCV educational materials and follow-up sessions for further discussion were offered.

Statistical analysis

Within the Networks II study, we identified individuals who had a baseline and at least two follow-up visits (and corresponding blood results for HCV serostatus) to generate three time points (in order to observe trends in injecting behaviour post HCV diagnosis). Two groups were defined. The 'Diagnosed during study' group comprised of individuals who received a new diagnosis of HCV during the study period. This included individuals who (i) serocon- verted during the study or (ii) were HCV RNA positive at study entry but stated at baseline interview that they had either never tested for HCV, or that they believed they were HCV negative. The 'Not diag- nosed during study' group comprised of the remaining individuals who did not receive a diagnosis of HCV during the study period, but

could still be anti-HCV or HCV RNA positive (if they were already aware of their HCV diagnosis when they entered the study).

Baseline characteristics of participants who had at least three time points were compared with participants who had less than three time points using a Wilcoxon rank-sum for continuous variables, and chi-square tests for categorical variables. Baseline characteristics of the 'Diagnosed during study' group, and the 'Not diagnosed during study' group were compared in the same manner. Associations between time since diagnosis, pre-diagnosis behaviour, and gender, and (i) injecting frequency and (ii) inject- ing equipment borrowing were investigated using generalized estimating equations (GEE). The study sample size limited multi- variable modelling to three concurrent predictors in any one model. Selection of the model correlation structure and model selection was undertaken using the Quasi-likelihood Information Criterion (QIC). All reported *p* values were exact and two-tailed, with $p < 0.05$ considered significant. All analyses were performed using STATA
version 11.0 (StataCorp, College Station, TX).

Results

Of 413 individuals enrolled in the cohort, 199 individuals had at least three data points for analysis. Those with three data points were comparable to those with less than three data points, except for median age (25.3 years and 26.0 years respectively, $p = 0.044$) (Table 1).

Amongst the 199 individuals, 35 individuals received a diagnosis of HCV, and 164 did not. Of the 35 individuals in the 'Diagnosed during study' group, 12 individuals seroconverted during the time period of the cohort, and 23 individuals received a diagnosis of HCV infection at baseline (blood test results at study entry showed HCV infection, but the participant stated at baseline interview that they were not aware of their HCV status or that they were HCV negative). The 23 who were already HCV RNA positive at study entry were comparable to those who seroconverted during the study, except for reporting longer injecting careers (median 10.3 years and 5.1 years respectively, $p = 0.040$). There were no significant differences between the characteristics of individuals in the 'Diagnosed during study' and the 'Not diagnosed during study' groups.

Injecting frequency in the 'Diagnosed during study' group

In univariable analysis, every one month since diagnosis of a positive HCV result was associated with a decrease of 0.48 injec- tions per month ($p = 0.016$). In the multivariable model, which corrected for pre-diagnosis injecting frequency and gender, every month since diagnosis was associated with a decrease of 0.35 injec- tions per month ($p = 0.046$) (Table 2).

Equipment borrowing in the 'Diagnosed during study' group

In the univariable analysis, there was no statistically signif- icant association between months since diagnosis and injecting equipment borrowing. This remained non-significant in the mul- tivariable model, which corrected for pre-diagnosis equipment borrowing and gender.

Separate multivariable models were used to investigate other variables, including age, length of injecting career and heroin use (data not shown), and all were non-significant.

Investigating potential cohort effects

We subsequently considered whether the observed reduc- tion in injecting risk behaviour in the 'Diagnosed during study' group was due to participation in the cohort. We therefore con- ducted a GEE analysis to examine the association between injecting

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Table 1
Characteristics of the 413 participants of the Networks II cohort.

Characteristic	Followed-up for	Not followed-up for three	*p* value	Diagnose d during	Not diagnosed	*p* value
Male (%)	126 (63.3%)	151 (70.6%)	0.118	26 (74.3)	100 (60.9)	0.19
Age at study entry (years)*	25.3 (22.4–29.8)	26.0 (23.2–30.2)	0.044	25.2 (23.4–28.2)	25.3 (22.2–29.8)	0.95
Age at first injection (years)*	17.0 (15.0–19.0)	17.0 (15.0–19.0)	0.136	17.1 (14.0–19.0)	17.8 (15.0–19.0)	0.46
Length of injecting career (years)*	8.3 (5.0–12.2)	8.6 (4.7–12.2)	0.910	9.3 (5.5–12.2)	8.1 (5.2–12.2)	0.56
Injected heroin most in last three	139 (70.2)	150 (70.4)	0.961	24 (68.6)	115 (70.1)	0.85
Born in Australia (%)	150 (75.4)	157 (74.1)	0.758	27 (77.1)	124 (75.6)	0.99
Received pharmacotherapy during study	101 (50.8)[a]	96 (44.9)[a]	0.231[a]	28 (80.0)	142 (86.6)	0.46
Baseline HCV antibody positivity (%)	130 (65.3%)	123 (70.3%)	0.306	23 (65.7)	107 (65.2)	0.99
Baseline frequency of injecting previous	20 (8.0–60.0)	25 (11.0–60.0)	0.066	40 (13.5–60.0)	24 (10.0–60.0)	0.16
Baseline frequency of borrowing in	0 (0–1.0)	0 (0–1.0)	0.925	0 (0–1.5)	0 (0–1.0)	0.47

Note: Data are presented as median (25–75% percentiles)* or *n* (%).

[a] Pharmacotherapy at baseline rather than during study period.

behaviour and time since study entry in the 'Diagnosed during study' group ($n = 35$) and the 'Not diagnosed during study' group ($n = 164$).

We found that the 'Diagnosed during study' group showed a significant reduction in injecting frequency over time since study entry ($p = 0.047$), but the 'Not diagnosed during study' group did not ($p = 0.093$). With regards equipment borrowing, we observed no significant change in either the 'Diagnosed during study' or the 'Not diagnosed during study' group ($p = 0.551$ and $p = 0.421$ respectively).

Table 2
Generalized estimating equation (GEE) analysis of the association between HCV diagnosis and the number of times injected and borrowed a fit in the months since diagnosis, in a cohort of 35 PWID.

Independent variable	Number of times injected in the months since diagnosis			Number of times borrowed a fit in the months since diagnosis		
	â coeff	95% CI	*p*	â coeff	95% CI	*p*
Months since HCV diagnosis	−0.35	(−0.68, 0.01)	0.046	0.002	(−0.012, 0.017)	0.750
Pre-diagnosis median number of times injected in last three months	0.28	(0.17, 0.40)	<0.001	0.37	(0.19, 0.55)	<0.001
Sex						
Female	1.00	–		1.00	–	
Male	−5.00	(−18.12, 8.12)	0.389	−0.50	(−1.10, 0.09)	0.095

Discussion

We observed a small reduction in injecting frequency but no change in injecting equipment borrowing following a diagnosis of HCV amongst a cohort of PWID in Melbourne, Australia. Previous studies have shown no change in injecting risk following a positive HCV test, although these studies had shorter periods of follow- up and did not examine injecting frequency (Aitken et al., 2004; Ompad et al., 2002; Tsui et al., 2009).

There were a number of limitations to our study. The sample size was small, and follow-up for at least three interviews was relatively low. The small sample size meant that it was not possible to account for a number of factors (such as opioid substitution ther- apy) that may have impacted on injecting behaviour. Further, it is not possible to rule out that the observed reduction in inject- ing frequency was due to a cohort effect, although we observed no significant reduction in injecting frequency over time since study entry in the 'Not diagnosed during study' group.

Amongst the 'Diagnosed during study group', only 12 individ- uals actually seroconverted during the study, and the remaining individuals were diagnosed with HCV infection at their base- line interview. Some individuals may therefore have already been aware of their diagnosis, even though they reported that they were unaware. Conversely, over half of the 'Not diagnosed during study group' were actually already HCV antibody positive, because they reported that they had received a diagnosis of HCV prior to entering the study. However, we might expect both of these limitations to dilute, rather than overestimate, the asso- ciation we have observed between HCV diagnosis and injecting behaviour.

The average reduction in injection frequency of 0.35 injections per month is small, although this reduction needs to be inter- preted in the context of the follow-up time across which this estimate was derived. An average reduction of 0.35 injections per month across the entire observation period (with a median follow-up of three years) translates into an average reduction of 12.6 injections across the three years. If starting from a base- line of 40 injections per month (which was the average baseline in our cohort), there would be a reduction to 27 injections per month by the end of the study period, a reduction of almost one-third.

However, a reduction in injecting frequency does not necessarily translate into a reduction in risk without a concurrent reduction in sharing episodes. We observed no significant change in needle and syringe borrowing in this study, although the level of borrowing at baseline was already very low. Qualitative evidence suggests that PWID diagnosed with HCV are less likely to be concerned about bor- rowing injecting equipment from others, on the assumption that they are already infected (Craine, Walker, Carnwath, & Klee, 2004). Counselling of HCV positive individuals should therefore empha- size the ongoing risk posed by other BBV, as well as the risk of onward transmission of HCV to other injecting partners. It might be expected that being diagnosed with HCV would have a greater impact on lending (rather than borrowing) of injecting equipment. However, the post hoc nature of this analysis meant we were unable to examine the impact of HCV diagnosis on injecting equipment lending.

We observed a small reduction in injecting frequency amongst a cohort of PWID diagnosed with HCV, over a five-year period offollow-up. This finding should be investigated further in larger studies examining a wider range of injecting risk behaviours.

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Disclosure

JG is on an advisory board for Merck, Sharp and Dohme.

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Contributors

EJA wrote the manuscript, AW contributed to the study design, undertook statistical analysis, and contributed to critical revisions of the manuscript; RSD contributed to study design and critical revisions of the manuscript; TS undertook statistical analysis and contributed to critical revisions of the manuscript; JG contributed to study design and critical revisions of the manuscript; PH con- tributed to study design and critical revisions of the manuscript; SJH contributed to study design and critical revisions of the manuscript, and MEH contributed to study design and critical revisions of the manuscript.

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