Hepatitis C testing and status among opioid substitution treatment clients in New South Wales

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Abstract

Background: In Australia about half of the people who inject drugs (PWID) are hepatitis C (HCV) antibody positive (anti-HCV+). The prevalence among opioid substitution treatment (OST) clients specifically is unclear, despite OST clinics being a potential setting for HCV care. This study aimed to report the prevalence of HCV among a large sample of NSW OST clients, understand whether HCV testing is translating into knowledge of status, and identify the correlates of inaccurate self-reporting of HCV status.

Methods: Participants completed an interview that included self-reported HCV status. Participants also provided a blood sample that was tested for HCV IgG antibodies, and for viral load using a quantitative real-time reverse-transcriptase polymerase chain reaction. Valid interviews and viable blood sample were provided by 1,484 participants. Logistic regression modelling was used to identify independent predictors of knowledge of HCV antibody status.

Results: Overall, 84% of participants were anti-HCV+. Of these, 65% were RNA+. Four per cent of anti-HCV negative participants were RNA+. One-quarter of anti-HCV+ participants did not know their status or reported it incorrectly, compared with 14.5% of anti-HCV negative participants.

Conclusion: The prevalence of HCV in this sample was higher than that found among other samples of people who inject drugs, suggesting the need for greater prevention efforts with OST clients. Anti-HCV+ individuals are less accurate at reporting their HCV status than those who are anti-HCV-. Inaccurate knowledge is associated with different variables for anti-HCV+ vs. anti-HCV- individuals. There are opportunities to improve knowledge of HCV status and to therefore improve health outcomes and reduce transmission among this at-risk population.

Key words: hepatitis C virus, HCV, injecting drug users, injecting risks, viral load

More than 220,000 Australians are living with chronic hepatitis C (HCV),[1] with more than half (~55%) of the Australians who inject drugs (PWID) estimated to be anti-HCV positive.[2] Liver disease is one of the largest contributors to mortality in this population,[3] with mortality among HCV-infected people now exceeding that among HIV-infected persons in the US.[4] Globally, liver cirrhosis accounts for 1.2% of disability adjusted life years (DALYs), with HCV accounting for about one-third of those.[5] This represents a 44% increase between 1990 and 2010. A recent estimate suggests that HCV attributable to injecting drug use added around half a million DALYs to the global burden of disease in 2010.[6]

Very few PWID currently seek HCV treatment, but dramatic improvements in treatment efficacy and reduced treatment length, complexity and toxicity are likely to increase treatment uptake among PWID in the future.[7,8] Australia has a well-established opioid substitution treatment (OST) program and many clinics offer blood-borne virus testing, but this is not necessarily delivered on-site,[9] limiting access for clients. OST clinics, however, provide a potential access point for HCV testing, management and treatment[10] and may play an important role in the roll-out of the new treatments in the future.[7]

The prevalence and incidence of HCV among PWID in Australia is well-established and decreasing.[11,12] However, there have been few recent prevalence studies of OST clients exclusively, who – given their longer injecting careers – are likely to have a higher prevalence than other drug injectors and consequently be in more immediate need of HCV management. It is important to determine both the prevalence of HCV among OST clients and their knowledge of their HCV status to ensure appropriate targeting and planning of future HCV screening and treatment activities. The current study uses a large sample of opioid dependent people recruited in New South Wales, Australia. The study aims are to:

1. Determine the prevalence of HCV infection (antibody and RNA status) among private and public OST clients in NSW.

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Submitted: June 2013; Revision requested: July 2013; Accepted: October 2013
The authors have stated they have no conflict of interest.
Aust NZ J Public Health. 2014; 38:160-4; doi: 10.1111/1753-6405.12173

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2. Identify differences in demographics, mental health, and substance use disorders between HCV antibody positive and negative participants.
3. Determine the accuracy of self-reported HCV status.
4. Identify predictors of inaccurate knowledge of HCV status.

Method

Procedure

This study used data from the Comorbidity and Trauma Study, a retrospective case-control study examining genetic and environmental factors contributing to opioid dependence liability.[13] Written informed consent was obtained from all participants. Ethics approval was obtained from the ethics committees of the University of New South Wales, Washington University, the Queensland Institute of Medical Research, and the area health service ethics committees governing the participating clinics. Participants were reimbursed $50 for out-of-pocket expenses. All participants received pre- and post-test counselling.

Participants

Participants (n=1,511) were recruited from public and private opioid pharmacotherapy clinics in the greater Sydney region between November 2005 and March 2008. Clinics were located in urban, suburban, regional and rural centres up to 180km from central Sydney.

Respondents were eligible if they were aged 18 years or over; had an adequate understanding of English; and had participated in opioid pharmacotherapy maintenance treatment for opioid dependence. Participants reporting recent suicidal intent or who were found to be currently experiencing psychosis were excluded from the study. HCV results and interview data were obtained for 1,484 of the 1,511 participants (both results were required to be included in the current analysis).

Structured interview

Detailed information regarding the structured interview has been published previously.[13] Each participant completed a face-to-face structured interview that provided lifetime *Diagnostic and Statistical Manual of Mental Disorders 4th Edition* (DSM-IV)[14] and *Diagnostic and Statistical Manual of Mental Disorders 3rd Edition, Revised* (DSM-III-R)[15] diagnoses for: heroin abuse and dependence; alcohol, cannabis, sedative, stimulants and cocaine abuse and dependence; nicotine dependence; post-traumatic stress disorder; major depressive episode; panic disorder; and antisocial personality disorder. These diagnoses were required to fulfill the aims of the study. The diagnostic sections of the interview were based on the Semi-Structured Assessment of the Genetics of Alcoholism – Australia (SSAGA-OZ).[16,17] There was an additional section on: age of first heroin use; age of first regular use; age of first dependence; age of first injecting; relapse to heroin use; imprisonment history; injecting drug use history; suicidality; heroin overdose; and heroin treatment history. Participants were asked "what is your current HCV status?" (positive, negative or don't know).

Blood sample

Providing a viable blood sample was necessary for participation. A venepuncturist took one to five 10 mL tubes of blood from each participant, depending on vein health. These samples were transferred on the day of collection to the Virology Laboratory at the Prince of Wales Hospital for processing. Plasma was tested for HCV IgG antibodies using the ADVIA Centaur HCV enzyme immunoassay (Siemens), according to manufacturer's instructions.

HCV antibody negative (anti-HCV-) samples were tested using a validated method in pools of five for HCV RNA using transposon mediated amplification (TMA, Versant Siemens). HCV antibody positive (anti-HCV+) samples were tested for HCV viral load using a quantitative real-time reverse-transcriptase polymerase chain reaction as described .[18]

Statistical analysis

Bivariate analyses were conducted using cross tabulations for dichotomous variables, and t-tests for continuous variables. Logistic regression models were run to compare those who correctly reported their HCV status to those who incorrectly reported it. Separate models were run for two groups of participants: (1) those who were anti-HCV-; and (2) those were anti-HCV+.

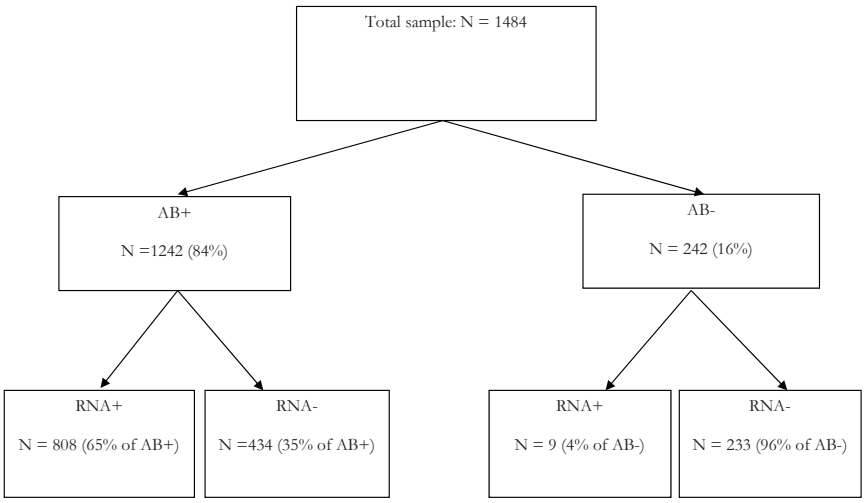
Variables were included in logistic regression models if $p<0.05$ in the bivariate comparisons. Age and sex were included to control for potential demographic differences. Non-significant variables were dropped from the final models. Alpha level was set at $p<0.05$. Results are reported in terms of odds ratios (OR) and 95% confidence intervals (95%CI) for categorical outcomes, and t-tests for continuous outcomes. All analyses were conducted in SPSS Statistics (v20).

Results

Prevalence of HCV

Eighty-four per cent of participants (n=1,242) were anti-HCV+ and, of these, 808 (65%) were RNA+. Nine anti-HCV- participants were RNA+, indicating recent infection (Figure 1). Of those who had been injecting for ≤1 year (n=44), 59% were anti-HCV+ compared with 87% of participants who had been injecting for >1 year (OR 3.16, 95%CI 2.16-4.62).

Figure 1: proportion of participants who are HCV AB +/- and RNA +/-.



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Sample characteristics: demographics, substance use and injection behaviours

Participants were typically in their mid to late 30s, had commenced opioid use prior to the age of 20 and first injected shortly after age 20 (Table 1). Ninety-nine per cent had ever injected drugs; 93% had injected drugs daily and reported an average of 15 years of injecting. The majority of participants were male, currently unemployed and had a prison history (Table 1). More than one-quarter had ever been paid for sex, almost half had ever injected in prison.

There were substantial demographic and drug use differences between anti-HCV positive and negative participants, with anti-HCV+ participants likely to be older, unemployed, to meet criteria for a range of substance use disorders, to have injected in prison, engaged in paid sex work, and have a more extensive opioid injecting career (Table 1). Those who were anti-HCV+ were also more likely to have spent time in prison, injected in prison or in illegal 'shooting galleries', be alcohol dependent, have experienced multiple overdoses and have engaged in paid sex work.

Awareness of HCV status

Of those who were anti-HCV+, almost a quarter (23%) either did not know their HCV status or thought they were anti-HCV-. Of those who were anti-HCV-, 15% thought they were anti-HCV+ or did not know their HCV status. Where participants were both anti-HCV+ and RNA+, 82% correctly reported their HCV status as positive.

Table 1: Demographic, mental health and drug use characteristics by HCV antibody status: unadjusted odds ratios.[a]

Variable	anti-HCV+ n=1242	anti-HCV- n=242	Total sample n=1484	OR (95% CI)
Unemployed (%)	84.7	73.1	82.8	2.03 (1.47-2.81)***
Sex (% male)	60.3	59.5	60.1	1.03 (0.78-1.37)
Married (%)	66.2	61.2	65.4	1.25 (0.94-1.66)
Ever injected any drug (%)	99.0	100	99.0	1.00 (1.00-1.00)
Injected daily (%)	96.1	75.2	92.7	8.20 (5.44-12.36)
Cannabis dependent (%)	54.8	58.7	55.4	0.85 (0.65-1.13)
Sedative dependent (%)	38.3	25.6	36.2	1.80 (1.32-2.46)***
Stimulant dependent (%)	50.8	45.9	50.0	1.22 (0.93-1.61)
Cocaine dependent (%)	34.2	20.7	32.0	1.99 (1.43-2.78)***
Alcohol dependent (%)	42.1	29.8	40.1	1.71 (1.27-2.31)***
Multiple opioid overdoses (%)	25.9	11.6	23.5	2.67 (1.76-4.03)***
Antisocial personality disorder (%)	52.4	59.9	53.6	0.74 (0.56-0.97)*
Major depressive episode (%)	60.8	67.1	61.9	0.76 (0.57-1.02)
Post-traumatic stress disorder (%)	51.1	43.1	49.8	1.38 (1.00-1.90)*
Borderline personality disorder (screener) (%)	59.6	53.3	58.6	1.29 (0.98-1.71)
Spent time in prison (%)	61.6	25.2	55.6	4.75 (3.48-6.49)***
Spent time in juvenile detention (%)	25.1	13.2	23.2	2.20 (1.49-3.27)***
Injected heroin >/=100 times (%)	96.5	88.4	95.4	3.63 (2.13-6.17)***
Injected in prison (%)	31.8	5.0	27.4	4.12 (2.16-7.82)***
Injected in shooting galleries (%)	44.5	26.4	41.3	1.68 (1.22-2.30)**
Engaged in sex work (%)	30.1	17.8	28.1	1.98 (1.39-2.81)***
Age in years (SD)	37.5 (8.5)	31.1 (7.0)	36.5 (8.6)	t=-12.54, df 393***
Length of injection career yrs (SD)	15.6 (8.8)	8.8 (6.0)	14.6 (8.8)	t=-13.51, df 436***
Age of first using heroin (SD)	19.3 (5.5)	20.3 (5.9)	19.5 (5.6)	t=2.31, df 1481*
Age of first injecting heroin (SD)	20.2 (6.0)	20.9 (5.2)	20.3 (5.9)	t=1.48, df 1425

** significant at p<0.05*
*** significant at p<0.01*
**** significant at p<0.001*
a bivariate odds ratios obtained by cross tabulation, t-statistic obtained by independent samples t-test

Predictors of incorrect reporting of anti-HCV status

In bivariate comparisons among anti-HCV+ participants, incorrect reporting was associated with being RNA-, being unmarried, no lifetime diagnosis of sedative dependence, and ever having injected drugs in prison. Among anti-HCV- participants, incorrect reporting was associated with being male, RNA-, and no lifetime diagnosis of stimulant dependence (Table 2).

Among anti-HCV+ participants, those who reported their anti-HCV status incorrectly were more likely to have started injecting opioids at an older age than those who knew their anti-HCV status (21.07 vs 19.92 years, t=-2.66, df 422, $p<0.01$) and to have had shorter injecting careers (14.05 vs 16.01 years, t=3.31, df 1,228, $p=0.001$). There was no difference in time spent in treatment (incorrect 44.2 months vs correct 48.8 months, t=1.21, df 1,215). Among anti-HCV- participants, those who reported their anti-HCV status incorrectly were more likely to have had shorter injecting careers (8.46 vs 10.9 years, t=2.05, df 195, $p=0.04$). There were no differences in age of onset for injecting opioids (21.1 vs 19.33 years, t=-1.73, df 195, $p=0.09$) or time spent in treatment (28 vs 39 months, t=1.19, df 30, $p=0.25$).

In the multivariate analysis for participants who were anti-HCV+, incorrect reporting was associated with being unmarried, RNA- and injecting drugs in prison, and weakly associated with a shorter injecting career. Among those who were anti-HCV-, males and those who were RNA- were more likely to incorrectly report their HCV status (Table 3).

Discussion

This study examined OST clients' HCV prevalence and their knowledge of their HCV status. The prevalence of anti-HCV among participants in this sample (84%), although higher than that found in other Australian (range 41% to 68%) and international studies of PWID (midpoint estimate of global prevalence 67%), is consistent with earlier Australian samples of OST clients.[19] This is the first large OST-specific assessment of HCV prevalence among OST clients since the reported overall decline of HCV incidence in Australia.[20]

The high prevalence found in this sample compared with studies of PWID indicates that more needs to be done to prevent HCV

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infections among OST clients. OST clinics can play an important role in delivering HCV treatment and care, especially once the more efficacious and less toxic treatment regimens are available.[7] Although participants were recruited through OST clinics that potentially provide an opportunity for routine blood-borne virus testing, one-in-five participants did not know their HCV status. The current finding may reflect earlier findings that onsite HCV testing is only routinely offered in less than half of Australian drug and alcohol agencies.[9]

Incorrect knowledge of HCV status for both anti-HCV+ and anti-HCV- individuals is likely to increase risky injecting practices.[21-23] Anti-HCV+ participants were more likely to have incorrect knowledge of their HCV status than anti-HCV- participants. Incorrect reporting among anti-HCV+ participants may be due to more recent infections, or because they were reporting their RNA status; anti-HCV+ participants who were RNA- were more likely to incorrectly report their antibody status as negative. Although technically incorrect, it suggests this group are aware of their actual HCV status but unfamiliar with the complexity of testing. It is also likely that some individuals misunderstood or forgot their most recent HCV test results.[24] However, as pointed out above, HCV testing of PWID is not always routine and in many instances it is likely that repeated antibody testing, including on those who have already tested positive, may have been undertaken with limited or absent RNA testing, potentially leaving people confused about their actual HCV status. Routine testing, while important, should be carried out for the benefit of the client.

Ever injecting drugs in prison also predicted incorrect reporting among this group. Although a weak association, a shorter injecting career was associated with incorrect

Table 3: Adjusted odds ratios for inaccurate anti-HCV knowledge.[a]

	Anti-HCV+ participants n= 1,230	Anti-HCV- participants n=242
Variable	**OR (95% CI)**	**OR (95% CI)**
Increasing age	1.00 (0.98-1.02)	0.97 (0.9.25-1.02)
Sex (male)	1.03 (0.78-1.37)	2.41(1.11-5.28)*
Married	0.72 (0.55-0.96)*	-
Increasing duration of injecting	0.98 (0.96-0.99)*	-
Injected in prison (ever)	1.47(1.07-2.01)*	-
RNA+	0.60 (0.44-0.81)***	0.06(0.01-0.26)***

a logistic regression model
** significant at p<0.05*
*** significant at p<0.01*
**** significant at p<0.001*

Table 2: Demographic and drug use characteristics by correct or incorrect reporting of HCV AB status: unadjusted odds ratios (N=1484)[a]

	Anti-HCV+			Anti-HCV-		
Variable (%)	**Correct reporting**	**Incorrect reporting**	**OR (95% CI)**	**Correct reporting**	**Incorrect reporting**	**OR (95% CI)**
RNA+	80.0	71.3	1.12 (1.04-1.21)**	20.0	1.4	13.8 (3.75-50.85)***
Male	61.0	57.0	1.04 (0.93-1.15)	42.9	62.3	0.45 (0.22-0.94)*
Unemployed	85.1	82.6	1.03 (0.97-1.09)	74.3	72.9	1.02 (0.82-1.26)
Married	67.6	60.8	1.26 (1.03-1.54)*	57.1	61.8	0.92 (0.68-1.26)
Cannabis dependent	55.2	53.6	1.07 (0.82-1.39)	59.4	56.0	1.06 (0.92-1.23)
Sedative dependent	40.2	32.1	1.42 (1.08-1.88)*	31.4	24.6	1.28 (0.74-2.20)
Stimulant dependent	51.2	50.9	1.01 (0.78-1.32)	62.9	43.0	1.46 (1.08-1.97)*
Cocaine dependent	34.3	33.4	1.04 (0.79-1.37)	20.0	20.8	0.96 (0.47-1.97)
Alcohol dependent	42.4	41.0	1.06 (0.81-1.38)	31.4	29.5	1.07 (0.63-1.82)
Antisocial personality disorder	52.4	52.8	1.01 (0.80-1.32)	65.7	58.9	1.12 (0.86-1.45)
Major depressive episode	60.2	63.2	1.13 (0.86-1.49)	71.4	66.3	1.08 (0.86-1.36)
Post-traumatic stress disorder	48.3	51.1	0.89 (0.66-1.21)	44.8	42.8	1.05 (0.67-1.63)
BPD (screener)	60.2	58.4	1.03 (0.93-1.15)	62.9	51.7	1.22 (0.91-1.62)
Spent time in prison	37.7	41.6	0.85 (0.65-1.11)	25.7	25.1	1.02 (0.56-1.88)
Injected for less than 1 year	1.6	4.2	0.37 (0.17-0.80)**	7.1	3.3	2.25 (0.94-5.36)
Injected heroin 100 or more times	97.0	94.8	1.02 (0.99-1.05)	90.0	88.1	1.02 (0.90-1.17)
Injected in prison ever	34.0	24.6	1.11 (1.04-1.18)**	8.6	4.3	1.97 (0.56-6.93)
Injected in shooting galleries ever	34.0	24.6	1.02 (0.96-1.09)	31.2	36.5	0.89 (0.74-1.07)
Currently in treatment	90.9	92.3	0.83 (0.09-7.81)	88.9	100.0	0.89 (0.71-1.12)
Age - years (SD)	37.8 (8.4)	37.0 (8.8)	t=1.32, df 1228	30.7 (6.6)	33.0 (8.7)	t=-1.38, df 31.4
Duration of injecting - years (SD)	16.0 (8.7)	14.1 (8.8)	t=3.31, df 1228***	8.5 (5.9)	10.9 (6.1)	t=-2.05, df 195*

a bivariate odds ratios obtained by cross tabulation
** significant at p<0.05*
*** significant at p<0.01*
**** significant at p<0.001*

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reporting of antibody status, perhaps due to fewer opportunities for HCV testing. Among anti-HCV- participants, incorrect reporting was associated with being male and being RNA+.

It is worth noting some important differences between anti-HCV+ participants and anti-HCV- participants. Those who tested anti-HCV+ were substantially more likely to have spent time in prison, injected in prison, juvenile detention or an illegal shooting gallery, engaged in paid sex work or experienced multiple overdoses, and to meet criteria for a number of substance use disorders. This group had engaged in a range of high-risk activities and, as such, a positive HCV test may indicate risk for a number of poor outcomes.

Limitations

This was a cross-sectional, retrospective study, limiting the extent to which we can make causal inferences. Participants were not asked how much time had elapsed since their last HCV test or how many times they had been tested. This variable might have explained some of the variation in knowledge of HCV status, since more recent testing is likely to provide a more accurate assessment of current HCV status.

Implications

The prevalence of HCV among OST clients in NSW (84%) is much higher than PWID (*cf* 50% NSP clients).[11] Australia has well-established treatment services for opioid dependence, which means this population should have good access to HCV testing and referral services. There is a need to understand why a significant number of these individuals reported their HCV status incorrectly. Improved access to BBV screening, ideally on-site, with appropriately targeted pre- and post-test counselling may improve HCV status knowledge among this group and provide important opportunities for management, prevention and treatment.

Conclusions

Anti-HCV among OST clients is much higher than that reported for PWID in New South Wales. Moreover, more than one-fifth of this large sample of OST clients did not know their HCV status, highlighting the need for better HCV testing and management of OST clients in NSW. Incorrect knowledge among both anti-HCV+ and anti-HCV- participants is likely to increase risky injecting behaviours.[21-23] Those who incorrectly believe themselves negative are unlikely to seek treatment for HCV. In both instances, improved knowledge of HCV status may lead to improved health outcomes and lower transmission rates.

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