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Determinants of hepatitis C antiviral effectiveness awareness among people who inject drugs in the direct-acting antiviral era

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ABSTRACT

Background & Aims: Although people who inject drugs (PWID) are at greatest risk of hepatitis C (HCV), treatment uptake in this population has historically been low. Highly effective direct acting antiviral (DAA) treatments for HCV have recently become available. Our aim was to assess the awareness among PWID of these new therapies and their effectiveness.

Methods: A national survey of PWID attending injecting equipment provision sites in Scotland during 2015-2016 included questions to gauge the awareness in this population of antiviral treatment and the high cure rates associated with new therapies (defined here as >80%).

Results: Among 2,623 PWID, 92% had ever been tested for HCV. After excluding those ever treated for HCV (n=226), 79% were aware of HCV treatment. Awareness was more likely among those who had ever been tested and self-reported either a positive (adjusted odds ratio: 16.04, 95%CI 10.57–24.33) or negative (3.11, 2.30–4.22) test result, compared to those who were never tested. The minority of all respondents (17%) were aware of high cure rates. This awareness was more likely among those who had ever been in HCV specialist care (9.76, 5.13–18.60) and those who had not been in specialist care but had been tested and self-reported either a positive (3.91, 2.20–7.53) or negative (2.55, 1.35–4.81) test result, compared to those who had never been tested.

Conclusion: We found poor awareness of the high cure rates associated with DAAs among PWID in Scotland, despite relatively high rates of HCV testing in this population. Increased effort is needed to ensure population groups with high risk of HCV infection are fully informed of the highly effective antiviral medications now available to treat this chronic disease.

INTRODUCTION

People who inject drugs (PWID) are at the greatest risk of hepatitis C virus (HCV) infection. Globally, there are an estimated 15.6 million (range: 10.2–23.7) individuals currently injecting drugs, of whom 52.3% (42.4–62.1%) have ever been infected with HCV [Degenhardt et al., 2017]. If left untreated, HCV can lead to severe complications of the liver including end stage liver disease and hepatocellular carcinoma; however, HCV is curable [Hajarizadeh, Grebely, Dore, 2013]. The therapeutic landscape of HCV has shifted greatly from less effective, often intolerable interferon-based therapy regimens into the highly anticipated era of direct acting antivirals (DAAs). New DAAs are associated with much optimism and enthusiasm as they are accompanied by high sustained viral response (SVR) rates (>90%), fewer and less severe side effects, simpler regimen, and shorter course duration [Dore, Feld, 2015; Gogela et al., 2015; Walker et al., 2015].

The World Health Organization (WHO) has published a global health sector strategy detailing the actions needed to work towards the elimination of viral hepatitis as a public health threat by 2030 [WHO, 2016], but this goal will only be achieved if those people at high risk of, or living with, infection have access to hepatitis prevention, diagnosis, and treatment services. Based on modelling studies which have illustrated the potential benefit of treating active PWID by reducing incidence through prevention of onward infections, EASL and WHO guidelines recommend the prioritization of HCV therapy among this group [Martin et al., 2011; Martin et al., 2013; EASL, 2015; WHO, 2016b]. Despite these guidance, the restriction of both active and recently abstinent PWID is a persistent barrier to initiation on to HCV therapy in Europe and elsewhere [Lazarus et al., 2017; Marshall et al., 2017; Ooka et al., 2017; Barua et al., 2015]. Access to treatment among those living with HCV could be further compromised if basic information about DAA treatment fails to reach PWID and other populations at high risk of infection and transmission.

Uptake of HCV-related prevention and care services among PWID, a traditionally difficult to reach population, has historically been limited due to a range of barriers operating at the patient, service provider, and system level [Paterson, Hirsch, Andres, 2013; Bruggmann, Grebely, 2015; Bruggmann, 2012]. Education of both patients and providers may help to address barriers preventing HCV care [Bruggmann, 2012; Marinho et al., 2016]. Research has suggested that adequate knowledge regarding HCV treatment may be an integral precursor to increased engagement with HCV-related care and treatment uptake [Marinho et al., 2016; Treloar et al., 2011]. In spite of this, data reporting the extent to which PWID are cognisant of the latest developments in HCV treatment, particularly their high cure rates, are scarce. Thus, herein, we used data from a national survey of PWID to examine knowledge of hepatitis C

treatment—and the individual-level characteristics associated with that knowledge—in the interferon-free therapeutic era. This study aims to identify if there are key gaps in knowledge of DAAs among PWID in Scotland, a country like many others which has initially prioritized DAAs to those with advanced liver disease, and inform the need for further interventions to address these potential gaps [Scottish Government, 2015; Lazarus et al., 2017; Marshall et al., 2017].

METHODS

Data sources

The Needle Exchange Surveillance Initiative (NESI) is a voluntary, anonymous, cross-sectional survey conducted biennially since 2008 to monitor HCV infection and related behaviours among PWID who assess injecting equipment provision (IEP) sites throughout mainland Scotland. Injection equipment provision in Scotland relates to both the distribution of needles and syringes and other injecting equipment, as described previously [NHS, 2017; Scottish Government, 2010]. Clients were approached at 118 IEP sites (relating to approximately 63% of all sites across the country) from February 2015-June 2016 and invited to participate if they had ever injected drugs [NHS, 2017]. Recruitment was done by trained interviewers who obtained informed consent prior to data collection. All surveyed participants were encouraged to submit a dried blood spot (DBS) sample to test anonymously for presence of HCV antibodies and RNA. Individuals who completed the survey received a £5 shopping voucher. NESI sampling and laboratory testing methods have been previously described [Allen et al., 2012]. Ethical approval for the NESI survey was granted by the NHS Health Research Authority Research Ethics Committee (REC Ref: 08/S0709/46).

Outcomes

Two outcome measures – on a) awareness of HCV treatment and b) knowledge of treatment effectiveness- were generated based on questions in the NESI survey conducted during 2015-2016, subsequent to the introduction of the first DAA therapies in Scotland in May 2014.

In relation to a), participants were asked if there is a treatment for hepatitis C; responses of *Yes* were compared to those reporting *No* or *Don't Know.* In relation to b), participants were asked "what are the chances of HCV being cured with current treatment?" with responses categorised as *Very High (81-100%), High (61-80%), Reasonable (41-60%), Low (21-40%), Very Low (0-20%),* and *Don't Know.* For our base-case analysis, we compared those responding *Very High (81-100%)* – in line with SVR rates typically observed with DAAs – to the rest.

Exposures of interest

We assessed outcomes according to relevant demographic and behavioural factors: (i) biological sex; (ii) age at survey (<35 years, 35+ years); (iii) NHS board of interview (Greater Glasgow & Clyde [GGC], outwith GGC); (iv) time since onset of injecting (<5 years, 5+ years); (v) history of recent injecting (injected >6 months previous to survey date, injected within 6 months previous to survey date); (vi) currently prescribed methadone; (vii) prisoner status (never imprisoned, imprisoned more than one year before survey date, imprisoned within one year of survey date); (viii) excessive alcohol use (<50 units per week, >50 units per week sustained for 12 months)[Brown et al., 2014]; and (ix) awareness of HCV infection status and uptake of HCV testing and care (never tested, ever tested and self-reported never HCV infected, ever tested and self-reported ever HCV infected but never attended HCV specialist care, ever tested and self-reported ever HCV infected and attended appointment at HCV care). Self-reported HCV diagnosis, as opposed to serology results, was examined to assess whether individuals who have been tested, diagnosed, and engaged with services have greater awareness of HCV treatment.

Analysis

Individuals were excluded if demographic data were insufficient or missing, resulting in 2,623 participants available for analysis.

Unadjusted and adjusted logistic regression was used to identify factors associated with a) HCV treatment awareness and b) the perceived effectiveness of HCV treatment as very high (defined as >80%). For our first analysis a), participants who were HCV treatment experienced were excluded. In relation to b), we restricted our population to those whose DBS test result indicated chronic infection (i.e. those eligible for antiviral therapy) in a supplementary analysis. Further, we also explored factors associated with the perceived effectiveness of HCV treatment as high (defined as >60%) in a sensitivity analysis.

All analyses were completed using Stata v.13.0 (StataCorp, College Station, TX, USA).

RESULTS

Participant characteristics

Among the 2,623 participants, the mean age at survey date was 38.2 years (standard deviation ±7.1 years; range 18.8–71.7 years) and 71% were male. Eighty-six percent had been injecting drugs for five of more years (median time injecting 14.3 years, IQR: 8.6–19.9 years) and the majority had injected within the 6 months previous to the survey date (82%). Of all participants, the vast majority (92%) had ever been tested for HCV, 40% reported they had ever

been diagnosed (44% of those ever tested), and 9% had a history of HCV treatment (relating to 21% of those who self-reported as having previously tested positive for HCV).

Awareness of HCV treatment

Of the 2,397 participants who had never received HCV treatment, 1,899 (79%) were aware that HCV treatment exists. Awareness of HCV treatment was highest among those who had been diagnosed with HCV and ever attended HCV specialist care (99%) and lowest for those who had reported never receiving a test (44%). (Table 1)

Factors associated with awareness of HCV treatment

The odds of HCV treatment awareness was greatest for those who had ever been tested for HCV and self-reported a positive test result/HCV infected (adjusted odds ratio [aOR] 16.04, 95% confidence interval [CI] 10.57–24.33) or negative test result/HCV uninfected (aOR 3.11, 95% CI 2.30–4.22), compared to those who had never been tested. (Table 2)

The odds of treatment awareness were also significantly higher for: females compared to males (aOR 1.30 95%CI 1.01–1.67); those who had commenced injecting 5+ years ago compared to those who had commenced within the previous 5 years (aOR 1.35, 95% CI 1.02–1.78); those who were currently prescribed methadone compared to those who were not (aOR 1.68, 95%CI 1.33–2.13); and those who had been imprisoned – within the last year (aOR 1.89, 95%CI 1.41–2.52) or more than one year ago (aOR 1.72, 95%CI 1.32–2.24) compared to those who were never imprisoned. While the odds of treatment awareness was lower for those interviewed within GGC NHS Board (aOR 0.78, 95% CI 0.62–0.98) compared to those interviewed elsewhere.

Awareness of very high HCV treatment effectiveness

The minority of survey participants (17%) perceived the effectiveness of HCV treatments as very high (defined as >80% cure rate). This perception was highest among those who had been diagnosed with HCV and have ever attended specialist HCV specialist care (35%) and lowest among those who had never been tested for HCV (5%). (Table 3)

Ninety one percent of those surveyed had a sufficient DBS sample for HCV RNA testing. Of those with a HCV RNA test result (n=2378), 879 (37%) were regarded as having chronic HCV infection at the time of survey (Appendix 2). Awareness of the very high effectiveness of HCV therapy was only marginally higher among those infected with chronic HCV (20%) compared to all participants (17%). (Appendix 2.1)

Factors associated with awareness of very high HCV treatment effectiveness

The odds of awareness of very high HCV treatment effectiveness was greatest for those who had been tested for HCV, self-reported a positive test result, and had attended a specialist service (aOR 9.76, 95%CI 5.13–18.59), for those who had been tested for HCV, self-reported a positive test result, but had never attended a specialist service (aOR 3.91, 95%CI 2.03–7.53), and for those who had been tested for HCV and self-reported a negative test result (aOR 2.56, 95%CI 1.36–4.81), compared to those who had never been tested. While the odds of awareness of very high HCV treatment effectiveness were significantly lower for those interviewed within GGC NHS Board (aOR 0.75, 95%CI 0.60–0.94) compared to those interviewed elsewhere. (Table 4)

When confined to only those with chronic HCV (n=879), the odds of awareness of very high HCV treatment effectiveness was similarly greater for those who had been tested for HCV, self-reported a positive test result, and had ever attended a specialist service (aOR 7.01, 95% CI 2.10–23.10), compared to those who had never been tested. (Appendix 2.2)

Sensitivity analysis

Thirty percent of participants perceived the effectiveness of HCV treatment as above 60%. In multivariate analysis, the odds of perceived HCV treatment effectiveness above 60% was greatest for those who had been tested for HCV, self-reported a positive test result, and had attended a specialist service (aOR 11.05, 95% CI 6.70–18.23), for those who had been tested for HCV, self-reported a positive test result, and had never attended a specialist service (aOR 4.40, 95%CI 2.66–7.28), and for those who had been tested for HCV and self-reported a negative test result (aOR 2.91, 95% CI 1.80–4.70), compared to those who had never been tested. (Appendix 1)

DISCUSSION

Our study shows that the majority of PWID in Scotland are aware that HCV is treatable, however more than 80% do not appreciate the high effectiveness of current therapies. Similarly, when we restricted this analysis to those with chronic HCV, only one in five know that HCV treatment is highly effective (defined as >80%).

To our knowledge, this is the first study to examine awareness of HCV treatment and its effectiveness among a large, national sample of active PWID in the DAA-era. Due to the high cost of new therapies and large numbers people of infected with HCV (~37,000 individuals, relating to 0.74% of the population), Scotland initially prioritised DAA treatment by disease stage *vis-à-vis* timing of treatment initiation [Scottish Government, 2015]. Consequently, efforts to raise awareness of the new HCV therapies among groups typically with mild HCV disease, such as PWID, may have been limited; however, Scotland's prioritization strategy does not

confine the prescription of DAA therapy to those with advanced disease. As such, approximately 40% of those initiated onto HCV treatment in 2015/16 in Scotland had mild, F0-F1 liver fibrosis [Scottish Government, 2015; data generated as part of HCV Quality Indicators, Health Protection Scotland]. Further, through implementation of the Scottish Government's HCV Action Plan (2008 onwards), once hailed by the Global Commission on Drug Policy as "an impressive example of a national strategy", Scotland considerably improved access to HCV testing and treatment services among PWID [Hutchinson et al., 2015; GCDP, 2013]. Therefore, we believe this work presents a contextual forewarning of the understanding of new HCV therapies among PWID which may be similar, or indeed worse, elsewhere.

Moreover, the population studied here had a reasonably high uptake of HCV testing (92% ever and 55% in the last year, among those who were not already diagnosed) and as such it was disappointing to find that the majority of PWID (66%) perceived treatment effectiveness to be low (≤40%; i.e. below that expected from interferon-based therapies) or did not know that HCV therapy is effective. Thus, the results highlight that additional efforts will be needed to ensure PWID and those at high risk of infection are fully informed of the new HCV therapies.

We observed an increase in treatment knowledge and awareness of DAA effectiveness associated with increased engagement with HCV service providers. Participants who had been tested for HCV and had ever attended a specialist service had the highest odds of awareness of HCV treatment effectiveness compared with those who had never received a test. However, PWID engagement with the HCV care cascade remains suboptimal [Bruggmann, 2015]. Forty-eight percent of our population who had self-reported a positive test result had ever attended an HCV specialist; therefore, more than half of those who had received a positive diagnosis for HCV had never engaged at the optimal level of care. Thus, there is a clear need for service providers outwith the specialist setting to equip PWID with information on HCV treatment and its effectiveness.

Education on therapies need not be limited to healthcare settings. In a recent survey among a group of former PWID attending Narcotics Anonymous (NA) in England, 30% were able to name new DAAs [Gilman, Littlewood, 2017]. This study also highlighted the negative perspectives of interferon that still exist and are shared amongst at-risk networks, indicating an immediate need to educate and shift the perspective of treatment. Negative views of interferon and its related side effects are persisting through the DAA era and have been shown to affect PWIDs' willingness to seek treatment [Mah et al., 2017; Whiteley et al., 2016]. Peer support and educational groups, such as NA, have been effective in linking PWID and former PWID with HCV

treatment and care [Gilman, Littlewood, 2017; Whiteley et al., 2016; Grebely et al., 2009] and could prove crucial in promoting the new HCV therapies.

Although our findings indicate that knowledge increases with service engagement, there remains a population who are most engaged (i.e. have received antiviral therapy) but remain uninformed. This has also been highlighted in a Scottish qualitative study which reports the lived experience of eight patients who were prescribed interferon-free therapies, and suggests that HCV treatment continues to be associated with the negative legacy left behind by interferon-based therapies. This qualitative assessment highlighted the need for improved and more educational rhetoric between patient and provider in relation to the evolved treatment regimens for HCV [Whiteley et al., 2016].

Hepatitis C-related educational sessions delivered in a harm reduction setting by both healthcare staff and peers has been shown to enhance HCV knowledge among PWID; however, these are most effective when coupled with action to address the social determinants of health inequity common in PWID populations [Galea et al., 2002; Norton et al., 2014; Mukherjee et al., 2017]. When successful, such educational interventions have been shown to positively influence attitudes toward engagement with HCV services and attitudes toward treatment [Treloar et al., 2011; Surjadi et al., 2011; Chen et al., 2013; Zeremski et al., 2014; Norton et al., 2014; Lafferty et al., 2016; Mukherjee et al., 2017]. Greater knowledge of HCV has been associated with a change in risk behaviour and engagement with the HCV care [Kwaikowski, Corsi, Booth, 2002]. Treatment willingness among those who are HCV infected has increased as diagnostic tools and treatments have become better tolerated [Alavi et al., 2015; Higgs, Hsieh, Hellard, 2015]. Accordingly, high HCV knowledge scores are associated with treatment willingness [Mah et al., 2017, Alavi et al., 2015; Shah et al., 2013; Gupta et al., 2007]. Thus, increasing the awareness of more tolerable and effective treatments may not only promote treatment willingness, but could also spur greater health service engagement and opportunity for health behaviour interventions which contribute to preventing transmission and/or disease progression among PWID.

Although measures have been taken to control for confounding, this study has limitations in respect to population and sampling bias. Our study is expected to over represent the true awareness of treatment effectiveness in the PWID population, as recruitment was done in a harm reduction setting, which also functions as a point of HCV care. Additionally, surveys such as NESI rely on participation willingness and self-report. Although self-report is considered a reliable source of data collection among people who use drugs [Darke, 1998], it is still reasonable to expect that some, albeit a minority of, participants provide what they perceive as

socially desirable answers to risk-related behavioural questions. Additionally, the 2015/16 NESI survey commenced in February 2015, eight months after the Scottish Medicines Consortium published approval of sofosbuvir, which may not have allowed sufficient time for therapeutic information to reach all PWID surveyed here [Scottish Medicines Consortium, 2014]. The 2017/18 NESI survey will contribute follow up data to determine if there has been a shift in HCV treatment-related knowledge as more time has elapsed since DAA approval in 2014 and interferon is phased out completely.

In spite of the great shift in the therapeutic landscape of HCV, what many consider a tremendous clinical advancement in medical history, our research suggests that the optimism regarding treatment may not have reached those infected or at risk of infection. Our study suggests an overall suboptimal awareness of DAA effectiveness among PWID exists in Scotland and highlights groups at all stages in the HCV continuum of care who should be targeted for educational interventions if the ambitions WHO HCV elimination goals are to be realised.

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AUTHOR CONTRIBUTIONS

AT, SJH, DJG, and AM conceived and designed the NESI survey. AM and AT implemented the survey. HV, NP, AMc, and SJH contributed to study conception and data analysis. HV, NP, AMc, HI, DJG, and SJH provided interpretation of findings. HV wrote the first draft of the manuscript, all remaining co-authors contributed to critical review and development of final manuscript.

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CONFLICT OF INTEREST STATEMENT

HI reports receipt of a speakers fee from Gilead Sciences in the past two years; DJG has received personal fees from Gilead Sciences, Bristol-Myers Squibb and Abbvie, all unrelated to this study. All remaining authors have nothing to disclose.

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TABLES

Table 1. Characteristics of 2,397 PWID surveyed during 2015/16 who had never received HCV antiviral treatment

Covariate	N † (col %)	Aware of HCV treatment (% of N)
All survey participants	2397 (100)	1899 (79)
Sex		
Male	1676 (70)	1312 (78)
Female	721 (30)	587 (81)
Age at survey		
<35	857 (36)	642 (75)
35+	1540 (64)	1257 (82)
Health board of interview		
Outwith-GGC	1549 (65)	1238 (80)
GGC	848 (35)	661 (78)
Time since onset of injecting (years)		
<5	356 (15)	229 (64)
5+	2041 (85)	1670 (82)
Injected in last 6 months		
No	433 (18)	357 (82)
Yes	1964 (82)	1542 (79)
Ever received methadone		
No	598 (25)	406 (68)
Yes	1799 (75)	1493 (83)
Excessive alcohol consumption		
No	2124 (89)	1682 (79)
Yes*	273 (11)	217 (79)
Prison history		
Never imprisoned	942 (39)	663 (70)
Imprisoned > 1 year ago	832 (35)	709 (85)
Imprisoned within last year	623 (26)	527 (85)
HCV test uptake, self-reported infection status, and attendance at HCV specialist care		
Never tested	233 (9)	98 (44)
Tested, not HCV infected	1338 (56)	1009 (75)
Tested, HCV infected, never attended clinic	545 (28)	503 (92)
Tested, HCV infected, ever attended clinic	291 (12)	289 (99)
Where last HCV tested (confined to those who have been HCV tested)		
GP	454 (21)	382 (84)
Drug Service	836 (38)	680 (81)
Hospital	410 (19)	333 (81)
Prison	408 (19)	348 (85)
Other	66 (3)	58 (88)

Abbreviations; HCV, hepatitis C virus; GGC, Greater Glasgow & Clyde; GP, general practitioner office

†Excluding patients who ever received treatment for HCV

*defined as consuming >50 units per week, sustained for 12 months

Table 2. Odds ratios for the awareness of HCV treatment among 2,397 PWID surveyed during 2015/16 survey participants who never received HCV antiviral treatment

Covariate	**Aware of HCV treatment**			
	Unadjusted OR (95% CI)	p-value	Adjusted OR (95%CI)	p-value
Sex				
Male	1.00		1.00	
Female	1.22 (0.97 – 1.52)	0.083	1.30 (1.01 – 1.67)	0.044
Age at Survey*				
<35	1.00			
35+	1.48 (1.21 – 1.82)	<0.001		
Health board of interview				
Outwith-GGC	1.00		1.00	
GGC	0.89 (0.72 – 1.09)	0.255	0.78 (0.62 – 0.98)	0.034
Time since onset of injecting (years)				
<5	1.00		1.00	
5+	2.50 (1.96 – 3.19)	<0.001	1.35 (1.02 – 1.78)	0.031
Injected in last 6 months				
No	1.00		1.00	
Yes	0.78 (0.59 – 1.01)	0.068	0.84 (0.63 – 1.13)	0.255
Ever received methadone				
No	1.00		1.00	
Yes	2.30 (1.87 – 2.85)	<0.001	1.68 (1.33 – 2.13)	<0.001
Excessive alcohol consumption				
No	1.00		1.00	
Yes*	1.01 (0.75 – 1.39)	0.909	0.90 (0.64 – 1.28)	0.564
Prison history				
Never imprisoned	1.00		1.00	
Imprisoned > 1 year ago	2.42 (1.91 – 3.07)	<0.001	1.72 (1.32 – 2.24)	<0.001
Imprisoned within last year	2.31 (1.78 – 2.99)	<0.001	1.89 (1.41 – 2.52)	<0.001
HCV test uptake and self-reported infection status				
Never tested	1.00		1.00	
Tested, not HCV infected	3.91 (2.92 - 5.24)	<0.001	3.11 (2.30 – 4.22)	<0.001
Tested, HCV infected	22.95 (15.35 - 34.34)	<0.001	16.04 (10.57 - 24.33)	<0.001

Abbreviations; HCV, hepatitis C virus; GGC, Greater Glasgow & Clyde; OR, odds ratio; aOR, adjusted odds-ratio; CI, confidence interval

Age at interview excluded from multivariate model due to collinearity with time since onset of injecting

Nearly 100% of the population attending HCV specialist services were aware of treatment, as such this exposure is not included in regression models.

*defined as consuming >50 units per week, sustained for 12 months

Table 3. Characteristics and perceived effectiveness of current HCV treatment among 2,623 PWID surveyed during 2015/16

Covariate	N (col %)	Perceived effectiveness of current HCV treatment (% of N)			
		Very High (81-100%)	**High (61-80%)**	**Reasonable (41 - 60%)**	**Low/DK (<41%)**
All survey participants	**2623**	**456 (17)**	**323 (12)**	**115 (4)**	**1729 (66)**
Sex					
Male	1862 (71)	332 (18)	238 (13)	76 (4)	1216 (65)
Female	761 (29)	124 (16)	85 (11)	39 (5)	513 (67)
Age at survey					
<35	917 (35)	141 (15)	91 (10)	31 (3)	654 (71)
35+	1706 (65)	315 (18)	232 (14)	84 (5)	1075 (63)
Health board of interview					
Outwith-GGC	1707 (65)	315 (18)	193 (11)	56 (3)	1143 (67)
GGC	916 (35)	141 (15)	130 (14)	59 (6)	586 (64)
Time since onset of injecting (years)					
<5	367 (14)	43 (12)	29 (8)	6 (2)	289 (79)
5+	2256 (86)	413 (18)	294 (13)	109 (5)	1440 (64)
Injected in last 6 months					
No	476 (18)	86 (18)	69 (14)	21 (4)	300 (63)
Yes	2147 (82)	370 (17)	254 (12)	94 (4)	1429 (67)
Ever received methadone					
No	644 (25)	98 (15)	72 (11)	21 (3)	453 (70)
Yes*	1979 (75)	358 (18)	251 (13)	94 (5)	1276 (64)
Excessive alcohol consumption					
No	2333 (89)	400 (17)	289 (12)	102 (4)	1542 (66)
Yes	290 (11)	56 (19)	34 (12)	13 (4)	187 (64)
Prison History					
Never imprisoned	1013 (39)	154 (15)	108 (11)	38 (4)	713 (70)
Imprisoned > 1 year ago	939 (36)	169 (18)	120 (13)	45 (5)	605 (64)
Imprisoned within last year	671 (25)	133 (20)	95 (14)	32 (5)	411 (61)
Test uptake, self-reported infection status, and attendance at HCV specialist care					
Never tested	223 (8)	11 (5)	9 (4)	3 (1)	200 (90)
Tested, not HCV infected	1340 (51)	167 (12)	142 (11)	54 (4)	977 (73)
Tested, HCV infected, never attended clinic	550 (21)	100 (18)	77 (14)	29 (5)	344 (63)
Tested, HCV infected, ever attended clinic	510 (19)	178 (35)	95 (19)	26 (6)	208 (41)

*defined as consuming >50 units per week, sustained for 12 months

Table 4. Odds ratios for the perceived effectiveness of HCV treatment as very high (defined as >80%) among 2,623 PWID surveyed during 2015/16

Covariate	**Perceived effectiveness of current HCV treatment as very high (81-100%)**			
	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Sex				
Male	1.00		1.00	
Female	0.89 (0.72 – 1.12)	0.346	0.94 (0.74 – 1.20)	0.621
Age at Survey*				
<35	1.00			
35+	1.24 (1.00 – 1.55)	0.047		
Health board of interview				
Outwith-GGC	1.00		1.00	
GGC	0.80 (0.65 – 0.99)	0.049	0.75 (0.60 – 0.94)	0.014
Time since onset of injecting (years)				
<5	1.00		1.00	
5+	1.68 (1.21 – 2.26)	0.002	1.19 (0.83 – 1.70)	0.342
Injected in last 6 months				
No	1.00		1.00	
Yes	0.94 (0.3 – 1.22)	0.664	0.90 (0.69 – 1.19)	0.470
Ever received methadone				
No	1.00		1.00	
Yes	1.23 (0.96 – 1.57)	0.095	1.04 (0.81 – 1.35)	0.723
Excessive alcohol consumption				
No	1.00		1.00	
Yes*	1.16 (0.85 – 1.58)	0.359	1.14 (0.82 – 1.58)	0.420
Prison History				
Never imprisoned	1.00		1.00	
Imprisoned > 1 year ago	1.22 (0.96 – 1.55)	0.097	0.95 (0.73 – 1.23)	0.682
Imprisoned within last year	1.38 (1.06 – 1.78)	0.014	1.19 (0.87 – 1.57)	0.232
Test uptake, self-reported infection status, and attendance at HCV specialist care				
Never tested	1.00		1.00	
Tested, not HCV infected	2.74 (1.47 – 5.13)	0.002	2.56 (1.36 – 4.81)	0.004
Tested, HCV infected, never attended clinic	4.28 (2.25 – 8.15)	<0.001	3.91 (2.03 – 7.53)	<0.001
Tested, HCV infected, ever attended clinic	10.33 (5.48 – 19.46)	<0.001	9.76 (5.13-18.59)	<0.001

Abbreviations; HCV, hepatitis C virus; GGC, Greater Glasgow & Clyde; OR, odds ratio; aOR, adjusted odds-ratio; CI, confidence interval

Age at interview excluded from multivariate model due to collinearity with time since onset of injecting

*defined as consuming >50 units per week, sustained for 12 months

SUPPORTING INFORMATION

APPENDIX 1. Odds ratios for the perceived effectiveness of HCV treatment as high (defined as >60%) among 2,623 PWID surveyed during 2015/16

Covariate	**Perceived effectiveness of current HCV treatment as high (61-100%)**			
	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Sex				
Male	1.00		1.00	
Female	0.85 (0.71 – 1.03)	0.109	0.89 (0.73 – 1.10)	0.280
Age at Survey*				
<35	1.00			
35+	1.39 (1.16 – 1.67)	<0.001		
Health board of interview				
Outwith-GGC	1.00		1.00	
GGC	0.99 (0.93 – 1.18)	0.926	0.95 (0.79 – 1.15)	0.610
Time since onset of injecting (years)				
<5	1.00		1.00	
5+	1.87 (1.42 – 2.45)	<0.001	1.33 (0.99 – 1.78)	0.055
Injected in last 6 months				
No	1.00		1.00	
Yes	0.85 (0.69 – 1.05)	0.131	0.81 (0.65 – 1.10)	0.067
Ever received methadone				
No	1.00		1.00	
Yes	1.24 (1.01 – 1.51)	0.035	1.02 (0.82 – 1.25)	0.882
Excessive alcohol consumption				
No	1.00		1.00	
Yes*	1.07 (0.82 – 1.40)	0.598	1.02 (0.77 – 1.35)	0.865
Prison History				
Never imprisoned	1.00		1.00	
Imprisoned > 1 year ago	1.27 (1.04 – 1.55)	0.016	0.93 (0.74 – 1.15)	0.495
Imprisoned within last year	1.47 (1.19 – 1.82)	<0.001	1.24 (0.98 – 1.58)	0.069
Test uptake, self-reported infection status, and attendance at HCV specialist care				
Never tested	1.00		1.00	
Tested, not HCV infected	3.01 (1.88 – 4.89)	<0.001	2.91 (1.80 – 4.70)	<0.001
Tested, HCV infected, never attended clinic	4.81 (2.94 – 7.89)	<0.001	4.40 (2.66 – 7.28)	<0.001
Tested, HCV infected, ever attended clinic	11.69 (7.15 – 19.10)	<0.001	11.05 (6.70 – 18.23)	<0.001

Age at interview excluded from multivariate model due to collinearity with time since onset of injecting

*defined as consuming >50 units per week, sustained for 12 months

Abbreviations; HCV, hepatitis C virus; GGC, Greater Glasgow & Clyde; OR, odds ratio; aOR, adjusted odds-ratio; CI,

APPENDIX 2 Serology results from HCV DBS and corresponding self-reported HCV status for 2,623 PWID surveyed during 2015/16

DBS HCV result	Self-reported HCV status		Total (%n*)
	Never Diagnosed	Ever Diagnosed	
Ab+ PCR+	318	561	879 (37)
Ab+ PCR-	156	263	419 (18)
Ab+ PCR NK	63	108	171 (NA)
Ab-	981	99	1080 (45)
NK	45	29	74 (NA)
Total	1563	1060	2623

*proportion confined to those with known result (n=2378)
Abbreviations; DBS, dried blood spot; HCV, hepatitis C virus; Ab, antibody; PCR, polymerase chain reaction

APPENDIX 2.1 Characteristics and perceived effectiveness of current HCV treatment among 879 PWID with chronic HCV infection surveyed during 2015/16

Covariate	N (col%)	Perceived effectiveness of current HCV treatment (% of N)			
		Very High (81-100%)	High (61-80%)	Reasonable (41 - 60%)	Low/DK (<41%)
HCV PCR +	879 (100)	183 (20)	127 (14)	39 (4)	530 (60)
Sex					
Male	650 (74)	139 (21)	98 (15)	27 (4)	386 (59)
Female	229 (26)	44 (19)	29 (13)	12 (5)	144 (63)
Age at survey					
<35	242 (28)	53 (22)	26 (11)	6 (2)	157 (65)
35+	637 (72)	130 (20)	101 (16)	33 (5)	373 (59)
Health board of interview					
Outwith GGC	496 (56)	111 (22)	64 (13)	12 (2)	309 (62)
GGC	383 (44)	72 (19)	63 (16)	27 (7)	221 (58)
Time since onset of injecting (years)					
<5	86 (10)	15 (17)	7 (8)	2 (2)	62 (72)
5+	793 (90)	168 (21)	120 (15)	37 (5)	468 (59)
Injected in last 6 months					
No	144 (16)	35 (24)	19 (13)	6 (4)	84 (58)
Yes	735 (84)	148 (20)	108 (15)	33 (4)	446 (61)
Ever received methadone					
No	206 (23)	43 (21)	31 (15)	5 (2)	127 (62)
Yes	673 (77)	140 (21)	96 (14)	34 (5)	403 (60)
Excessive alcohol consumption					
No	757 (86)	156 (21)	109 (14)	32 (4)	460 (61)
Yes*	122 (14)	27 (22)	18 (15)	7 (6)	70 (57)
Prison history					
Never imprisoned	253 (29)	64 (25)	29 (11)	10 (4)	150 (59)
Imprisoned >1 year ago	362 (41)	58 (16)	56 (15)	18 (5)	230 (64)
Imprisoned within last year	264 (30)	61 (23)	42 (16)	11 (4)	150 (57)
Test uptake, self-reported infection status, and attendance at HCV specialist care					
Never tested	47 (5)	3 (6)	4 (8)	1 (2)	39 (83)
Tested, not HCV infected	271 (31)	42 (15)	30 (11)	11 (5)	188 (69)
Tested, HCV infected, never attended clinic	262 (30)	46 (18)	34 (13)	8 (3)	174 (66)
Tested, HCV infected, ever attended clinic	299 (34)	92 (31)	59 (18)	19 (6)	129 (73)

*defined as consuming >50 units per week, sustained for 12 months
Abbreviations; HCV, hepatitis C virus; GGC, Greater Glasgow & Clyde

Appendix 2.2 Odds ratios for the perceived effectiveness of current HCV treatment as very high (defined as >80%) among 879 PWID with chronic HCV infection surveyed during 2015/16

Covariate	Perceived effectiveness of current HCV treatment as very high (81-100%)			
	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Sex				
Male	1.00		1.00	
Female	0.87 (0.60 – 1.28)	0.487	0.78 (0.20 – 1.17)	0.234
Age at Survey*				
<35	1.00			
35+	0.91 (0.64 – 1.31)	0.626		
Health board of interview				
Outwith-GGC	1.00		1.00	
GGC	0.80 (0.58 – 1.12)	0.195	0.79 (0.56 -1.12)	0.181
Time since onset of injecting (years)				
<5	1.00		1.00	
5+	1.27 (0.71 – 2.28)	0.418	1.19 (0.64 – 2.22)	0.576
Injected in last 6 months				
No	1.00		1.00	
Yes	0.78 (0.51 – 1.20)	0.261	0.72 (0.46 – 1.12)	0.144
Ever received methadone				
No	1.00		1.00	
Yes	0.99 (0.69 – 1.46)	0.982	0.92 (0.61 – 1.38)	0.695
Excessive alcohol consumption				
No	1.00		1.00	
Yes*	1.09 (0.69 – 1.74)	0.701	1.19 (0.73 – 1.92)	0.479
Prison History				
Never imprisoned	1.00		1.00	
Imprisoned > 1 year ago	0.56 (0.38 – 0.84)	0.005	0.48 (0.31 – 0.74)	0.001
Imprisoned within last year	0.88 (0.59 – 1.32)	0.561	0.82 (0.53 – 1.28)	0.388
Test uptake, self-reported infection status, and attendance at HCV specialist care				
Never tested	1.00		1.00	
Tested, not HCV infected	2.69 (0.80 – 9.06)	0.110	2.61 (0.77 – 8.55)	0.124
Tested, HCV infected, never attended clinic	3.12 (0.93 – 10.50)	0.066	3.16 (0.93 – 10.72)	0.065
Tested, HCV infected, attended clinic	6.51 (1.97 – 21.53)	0.002	7.01 (2.10 – 23.10)	0.002

Age at interview excluded from multivariate model due to collinearity with time since onset of injecting

*defined as consuming >50 units per week, sustained for 12 months

Abbreviations; HCV, hepatitis C virus; GGC, Greater Glasgow & Clyde; OR, odds ratio; aOR, adjusted odds-ratio; CI, confidence interval