DE GRUYTER OPEN

Original Article

Exploring patient characteristics and barriers to Hepatitis C treatment in patients on opioid substitution treatment attending a community based fibro-scanning clinic

Des Crowley[1], Walter Cullen[2], Eamon Laird[3], John S. Lambert[4], Tina Mc Hugh[5], Carol Murphy[6], Marie Claire Van Hout[7]

[1] Addiction Services HSE, Dublin 7, Ireland;
[2] University College Dublin, Dublin 4, Ireland;
[3] Trinity College Dublin, University College Dublin, Dublin 2, Ireland;
[4] Infectious Disease Department, Mater Hospital, Dublin 7, Ireland;
[5] Mater Hospital, Dublin, Ireland;
[6] Infectious Disease Department, Mater Hospital, Dublin 7, Ireland;
[7] Public Health Institute, Liverpool John Moore's University, Liverpool, United Kingdom

ABSTRACT

Background and Objectives: Hepatitis C virus (HCV) infection is a major public health issue. There is substandard uptake in HCV assessment and treatment among people who inject drugs (PWID). Community fibroscanning is used to assess disease severity and target treatment. **Methods**: A survey was administered to a cohort of chronically HCV infected patients attending a community fibroscanning clinic. Questions targeted diagnosis of HCV, suitability, willingness and barriers to engagement in treatment. Descriptive and regression analysis, with thematic analysis of open-ended data was conducted. **Results**: There was high acceptance of community fibroscanning among this cohort with over 90% (68) attending. High levels of unemployment (90%) and homelessness (40%) were identified. Most patients were on methadone treatment and had been HCV infected for greater than 10 years with length of time since HCV diagnosis being significantly longer in patients with fibroscan scores > 8.5 kPa ($P = 0.016$). With each unit increase in methadone dose, the odds of the >8.5 fibroscan group increased by 5.2%. Patient identified barriers to engagement were alcohol and drug use, fear of HCV treatment and liver biopsy, imprisonment, distance to hospital and early morning appointments. **Conclusion**: The study highlights the usefulness of community fibroscanning. Identifying barriers to treatment in this cohort affords an opportunity to increase the treatment uptake. The availability of afternoon clinics and enhanced prison linkage are warranted.

Address for Correspondence:
Dr. Marie Claire Van Hout, Ph.D., Professor of Public Health Policy, Public Health Institute, Liverpool John Moore's University, Liverpool, United Kingdom.
Email: m.c.vanhout@ljmu.ac.uk

Access this article online

Website: www.intern-med.com

DOI: 10.1515/jtim-2017-0017

Quick Response Code:

Key words: hepatitis C virus, drug users, opiate substitution treatments, blood borne virus, fibroscan

INTRODUCTION

Hepatitis C virus (HCV) infection remains a major public health burden. It is spread by contact with infected blood or other bodily fluids.[1-6] An estimated 185 million people are infected with HCV globally[7] with a reported 15 million Europeans living with HCV infection.[8, 9] Chronic disease outcomes occur in 55-85% of untreated cases, and center around an impaired quality of life, liver cirrhosis, liver failure and hepatocellular carcinoma.[10, 11] Injecting drug use remains a significant driver of the European HCV epidemic with estimates that HCV antibody prevalence among persons who inject drugs (PWID) in 29 European countries ranges from 5% to 90% with growing rates of HCV among new injectors of novel psychoactive substances (NPS).[8,12-13]

There is a high prevalence of HCV within the aging PWID population, characterized

by many undiagnosed cases and failure to access treatment [14] Surveillance and monitoring of HCV in Europe, particularly regarding levels of antiviral treatment uptake among PWID are limited.[15-17] Recent increases in HCV infection among PWID in some European countries are reported despite increased efforts to upscale the HCV cascade of care.[18,19]

Low rates of HCV treatment uptake and sub-optimal access are reported among PWID.[6, 9, 20-22] PWID encounter significant barriers to accessing the HCV treatment[15,23] and are often denied treatment due to concerns around the on-going risk behavior despite treatment reducing further transmission.[6, 23, 24] HCV treatment outcomes in PWID are comparable to general population patients with no history of drug use.[23,25-27] Despite suboptimal access and uptake, research demonstrates a PWID interest in HCV treatment.[28-32]

Up to recently, the standard treatment for chronic HCV infection was pegylated interferon (PEG-IFN) and ribavirin (RBV).[33] The development of new drug therapies includes protease and polymerase inhibitors (DAAs) that are well tolerated, do not require liver biopsy and have minimal side effects. Liver biopsy whilst evident as the gold standard of liver fibrosis is difficult, invasive and costly.[34] Liver stiffness measurement (LSM) using fibroscan is increasingly being used to assess disease severity.[35] This procedure can help to enhance HCV assessment, reduce treatment barriers, triage patients and target therapy.[14, 36] Several studies have reported on the feasibility of fibroscanning as a screening tool for drug users, with high rates of acceptance and uptake within various treatment and street outreach settings.[37-41]

In Ireland, an estimated 20,000-50,000 people have been exposed to HCV infection, giving a prevalence rate of 1-2%.[42] Most recent prevalence data of HCV in the Irish PWID population ranges from 62-81%[42, 43] with risk factors similar to those reported elsewhere. These are injecting drug use,[42, 43-47] frequency and length of time injecting,[45, 48, 49] needle sharing and having a history of imprisonment.[45] Low uptake of screening and follow up assessments are also reported.[51-53] In Ireland, the treatment with DAAs is restricted to those with more advanced liver disease, determined by fibroscan score, with current guidelines identifying those with scores of > 8.5 kPa as being eligible for the treatment.

METHODS

The aim of the study was to report on characteristics of OST patients attending a community based fibroscanning clinic, and their reported barriers to engaging with HVC treatment in Ireland. The fibroscanning clinic took place in The City Clinic, the largest community based drug treatment center in Ireland. This center provides OST to 300 opioid dependent patients living in the North inner city area of Dublin, an area of social deprivation. Patients entering OST are offered viral screening within a month of starting the treatment and post a risk behavior thereafter. A viral screen audit was completed to identify patients with chronic HCV infection, who had not successfully completed the HCV treatment in the past and who would benefit from an assessment by fibroscan (n=80).

The data collection tool was designed based on consultation with the literature and team review. The instrument contained a series of descriptive questions collecting data on gender, age, employment status, dose and length of time on methadone, length of time since/location of HCV diagnosis, if referred/attended hospital for follow up, if ever had a biopsy and if previously offered / completed HCV treatment. Patients were asked a series of open ended questions around HCV symptoms experienced, self-reported drug and alcohol stability, reasons for non-attendance, factors contributing to non-attendance and potential facilitators for treatment engagement.

Ethical approval was given by The Mater Hospital, Dublin, Ireland as part of the European HepCare Project. Patients were given an information sheet on the study and provided written consent. The questionnaire was administered by a research assistant who accompanied the nurse specialist performing the fibroscan.

Anonymized data yielded descriptive statistics (frequencies, percentages) to summarize the participant characteristics. Statistical tests using SPSS including the Chi square tests, t-tests and P-values were used to assess the differences in categorical data, with a significance level of 0.05. Multi-nominal logistic regression analysis was used to determine predictors of answer responses with the neutral response category as the reference. Qualitative open ended comment data were thematically coded for common and emergent themes using QSR –NVIVO-10.

RESULTS

Participant profile

The mean age of the participants was 39 years with no significant difference between men and women. A high proportion of patients described their accommodation as not stable (40%) and only 9% were engaged in some form of employment. The average methadone dose was 75 mL with an average of 10 years on MMT (Table 1) with again no difference between men and women. The majority of participants (71%) self-declared ongoing/drug or alcohol

instability as a factor impacting their ability to engage with the HCV assessment and treatment.

On an average, the study population was diagnosed with Hepatitis C for 10.5 years, with just less than half (47%) describing having symptoms related to HCV infection. Over half the group (57%) had previously been offered a hospital appointment for HCV follow-up with most attending (54%). Less than a third (27%) of the group had a previous liver biopsy or fibroscan. Of this group, only thirteen patients had been assessed as suitable for treatment with significantly more men than women being told they were suitable for interferon based treatment (26% *vs.* 0%; *P*=0.016) (Table 2), but none of these had been engaged.

Fibro scanning results (Tables 3 and 4)

The average Fibro scan score was 6.4 kPa. Almost a third of this cohort had Fibro scan sore > 8.5 kPa, with a slightly higher proportion of men (38%) compared to women (16.6%) reaching this score but this failed to reach statistical significance (*P*=0.072). Over 20% of patients had a fibroscan score of > 12.5 kPa. Importantly, there was no significant difference between patients experiencing self-declared HCV related symptoms and their fibroscan score [> 8.5 (*P*=0.5) (Table 3), > 12.5 kPa (*P*=0.2) (Table 4)]. Participants with a Fibro scan score > 8.5 kPa were diagnosed with having Hepatitis C for a significantly longer period than those with a san score < 8.5 kPa (15 years *vs.* 10 years, *P* = 0.016, Table 3). Homelessness, employment status, length of time on MMT, patients experiencing HCV related symptoms and self-declared drug and alcohol

Table 1: Population characteristics by gender

	Total (*n*=68)	Male (*n*= 50)	Female (*n*= 18)	*P*-Value
Age (years)	39.0 (35.2, 44.0)	40.0 (35.0, 45.0)	39.0 (35.7, 42.0)	0.882
Accommodation status stable % (*n*)	61.7 (42)	58.0 (29)	72.2 (13)	0.366
Engaged in work % (*n*)	8.8 (6)	6.0 (3)	16.6 (3)	0.201
Time on MMT (years)	10.0 (5.0, 19.5)	10.0 (5.0, 19.2)	12.5 (6.2, 19.5)	0.773
Methadone dose (mL)	75.0 (47.0, 90.0)	75.0 (50.0, 90.0)	70.0 (43.7, 90.0)	0.251
Alcohol /drug unstable (self-declared) % (*n*)	70.5 (48)	70.0 (35)	72.2 (13)	0.913

Values are median (25^{th}–75^{th} percentile) or % (*n*). Continuous variables assessed by independent *T*-test; Categorical variables assessed by Chi-square analysis. MMT: methadone maintenance treatment. *P*<0.05 were considered statistically significant.

Table 2: Population characteristics by HCV issues and gender

	Total (*n*=68)	Male (*n*= 50)	Female (*n*=18)	*P*-Value
Diagnosed hepatitis C (years)	10.5 (8.0, 16.2)	10.0 (7.7, 17.0)	12.5 (9.0, 6.7)	0.817
Symptoms related to hepatitis C % (*n*)	47.0 (32)	42.0 (21)	61.1 (11)	0.172
Offered OPD appointment % (*n*)	57.3 (39)	60.0 (30)	50.0 (9)	0.414
Attend OPD appointment % (*n*)	54.4 (37)	54.0 (27)	55.5 (10)	0.906
Previous liver biopsy or Fibroscan % (*n*)	29.4 (20)	32.0 (16)	22.2 (4)	0.348
Fibroscan result (kPa)	6.4 (5.2, 10.1)	7.2 (5.3, 11.8)	5.6 (5.2, 6.7)	0.104
Previously assessed suitable for treatment % (*n*)	19.1 (13)	26.0 (13)	0	0.016
Fibroscan result >8.55 (kPa) % (*n*)	32.3 (22)	38.0 (19)	16.6 (3)	0.072
Fibroscan result >12.5 (kPa) % (*n*)	20.3 (12)	20.0 (10)	11.1 (2)	0.362

Values are median (25^{th}–75^{th} percentile) or % (*n*). Continuous variables assessed by independent *T*-test; Categorical variables assessed by Chi-square. HCV: hepatitis C virus. *P*<0.05 were considered statistically significant.

Table 3: Fibro scan score population characteristics (>8.5 kPa)

	Fibro scan score		
	<8.5 (*n*=37)	>8.5 (*n*=22)	*P*-Value
Age (years)	39.0 (35.0, 42.5)	40.0 (36.0, 45.2)	0.339
Accommodation status stable %(*n*)	64.8 (24)	59.0 (13)	0.404
Engaged in work %(*n*)	8.1 (3)	9.0 (2)	0.965
Time on MMT (years)	10.0 (5.0, 17.0)	10.0 (2.0, 20.0)	0.921
Methadone dose (mL)	60.0 (40.0, 82.5)	80.0 (63.7, 95.0)	0.072
Diagnosed hepatitis C (years)	10.0 (6.0, 15.0)	15.0 (8.5, 20.0)	0.016
Having symptoms related to hepatitis C (self-declared) % (*n*)	43.2 (16)	50.0 (11)	0.513
Alcohol /drug unstable (self-declared) % (*n*)	67.5 (25)	77.2 (17)	0.941

Values are median (25^{th}–75^{th} percentile) or % (*n*). Continuous variables assessed by independent *T*-test; Categorical variables assessed by Chi-square analysis. MMT: methadone maintenance treatment. *P*<0.05 were considered statistically significant.

stability seemed to have no impact on a patient having a fibro scan score > 8.5 kPa and being eligible for treatment with DAAs in Ireland. Of particular interest is that with each unit increase in methadone dose, the odds of being in the > 8.5 Fibroscan group increased by 5.2 % (Table 5)

Thematic analysis

HCV symptoms experienced

A majority of participants (70%) self-reported drug instability. Participants reported use of excess alcohol, smoking of opiates and crack cocaine and use of benzodiazepines, with a minority reporting continued IDU of heroin. A minority reported daily or problematic use of alcohol. HCV symptoms experienced included abdominal pain, stomach bloating, fatigue, anxiety, weight gain, swelling of the limbs and a yellow tinge to the skin (Table 5). Some participants were not aware of any HCV symptoms. A majority of those with fibroscan scores of > 8.5 kPa were not aware of HCV symptoms other than fatigue (Beta = 0.051, Exp (B) = 1.052, $P = 0.026$, 95% CI (1.006-1.1).

Barriers to attendance

Individual patient reasons for not initially attending the HCV clinic centered around on-going drug and alcohol use, on-going injecting drug use, not wanting to have treatment at the time, fear around invasive HCV and treatment interventions and addiction treatment relapse. Many narratives illustrated lack of readiness for treatment of HCV. One participant described being too ill from interferon to attend the clinic. Of particular note were the significant barriers reported by those with a fibroscan score of > 8.5 kPa, which centered on the inability to engage with HCV treatment and care due to custodial sentencing, poor prison referrals, parental bereavement and chaotic family and drug using lifestyles. Many participants also described chaotic personal and family lifestyles, and lengthy distance from the clinic making treatment adherence and attendance at early appointments difficult to commit to.

Enablers to treatment

When questioned about the facilitators to ensure continued engagement with HCV treatment, participants described structural barriers that included problems when no follow-up appointments were kept. This may have been due to clinic staff concern around chaotic lifestyles and on-going drug and injecting drug use, or appointments provided and not attended. Afternoon appointments, enhanced prison referral mechanisms into the community fibroscanning unit, and the location of services within the addiction treatment and detoxification services were viewed as potentially useful.

DISCUSSION

The study presented a unique Irish profile of OST patients accessing a community based fibro-scanning clinic in Dublin, Ireland. The participants in this study reflect an

Table 4: Fibro scan score population characteristics (>12.5 kPa)

	Fibro scan score		
	<12.5 (*n*=47)	**>12.5 (*n*=12)**	***P*-Value**
Age (years)	39.0 (35.0, 43.0)	40.5 (36.0, 46.0)	0.301
Accommodation status stable%(*n*)	59.5 (28)	75.0 (9)	0.584
Engaged in work % (*n*)	10.6 (5)	0 (0)	0.170
Time on MMT (years)	10.0 (4.2, 15.2)	20.0 (9.2, 25.0)	0.179
Methadone dose (mL)	65.0 (45.0, 80.0)	90.0 (72.5, 98.7)	0.091
Diagnosed hepatitis C (years)	10.0 (7.0, 15.0)	17.0 (14.0, 20.0)	0.012
Having symptoms related to Hepatitis C (self-declared) % (*n*)	40.4 (19)	66.6 (8)	0.244
Alcohol /drug unstable (self-declared) % (*n*)	72.3 (34)	66.6 (8)	0.294

Values are median (25^{th}–75^{th} percentile) or % (*n*). Continuous variables assessed by independent *T*-test; categorical variables assessed by chi-square analysis. MMT: methadone maintenance treatment. $P<0.05$ were considered statistically significant.

Table 5: Predictor's of fibroscan scores

	Unstandardized coefficients			95% Confidence interval	
Variable	B	Std. Error	*P*-value	Lower	Upper
Age	0.13	0.35	0.717	-0.58	0.83
Gender	3.64	4.06	0.377	-4.63	11.90
Methadone dose (mL)	0.16	0.08	0.049	0.00	0.31
Years diagnosed Hepatitis C (years)	0.21	0.32	0.506	-0.43	0.85

Linear regression analysis

aging cohort of PWIDs with a mean age of 39 years, with high levels of unemployment (> 90%) and homelessness (40%) on long term MMT (> 10 years) and having a diagnosis of untreated chronic HCV infection for over a decade. A majority of patients (*n* = 70%) described the ongoing issues of drug and alcohol instability that impacted their ability to engage with HCV services. This group was traditionally seen as hard to reach group for engagement with health services and in particular with HCV screening, assessment and treatment.[9,14,21-23] This study shows that when screening and fibro scanning are offered at drug treatment locations, patients will engage in these services (*n*= 85%).[54]

The average fibro scan score in this cohort was 6.4 kPa, which is similar to that found in other studies.[39,41] Just under a third of participants had scores > 8.5 kPa (30%) indicating at least moderate fibrosis and eligible for DAAs in accordance with Irish HCV treatment criteria. 20% of the cohort had a score > 12.5 kPa, indicative of cirrhosis. Of interest is that self-declared HCV related symptoms were no different in those with normal scores (< 8.5 kPa) compared to those with scores indicative of fibrosis (> 8.5 kPa) and cirrhosis (> 12.5 kPa). This is an important finding showing that patients may not be aware of the severity of their liver disease and may have developed significant levels of fibrosis and cirrhosis before these are identified by treatment services.[11] It may also reflect the high levels of other disease morbidities seen in this group along with symptoms of drug and alcohol withdrawals that may mask symptoms of chronic HCV infection.

As expected, the patients with scores > 8.5 kPa were diagnosed with HCV significantly longer than those with a scores < 8.5 kPa (*P*=0.16). This reflects the progression of liver disease over time after HCV exposure.[10] Contrary to what might be expected, the impact of self-declared drug and alcohol instability did not have a significant impact on fibroscan score. Ongoing alcohol misuse in chronically HCV infected individuals is associated with more severe liver disease.[10] Separating drug and alcohol stability as risks may have yielded a different result, but this finding is in keeping with poly-drug use pattern of this cohort and the tendency to substitute alcohol and illicit drug use over a lifetime of addiction and drug abuse. The high levels of self-declared drug and alcohol stability are also of interest. Despite patients receiving therapeutic doses of methadone maintenance treatment (MMT, average dose 75mL) for long periods of time (>10 years) 70% indicated that drug / alcohol instability affected their ability to engage with HCV services. This may reflect the level of social exclusion (90% unemployment) of this group and supports the provision of augmented rehabilitation and support services to this marginalized group.

A unique finding of this study was that with each unit increase in methadone dose, the odds of being in the > 8.5 Fibroscan group increased by 5.2%. To our knowledge, this has not been previously reported. This may indicate that the patients requiring higher doses of methadone are at greater risk of developing more severe liver disease and can potentially be used to target higher risk groups among PWIDs for HCV treatment interventions.

Previous studies have illustrated how barriers to effective HCV care among Irish PWID center on negative experiences at diagnosis, investigations and treatment [35] Findings in this study described patient reluctance to engage with HCV assessment due to ongoing alcohol and drug use, injecting drug use, OST treatment relapse, fear around HCV and invasive treatment interventions and inability to attend due to custodial sentencing and lack of prison referral. Barriers to continued engagement centered on illness, distance from the treatment setting, early appointments and lack of follow up appointments, potentially due to staff concerns around on-going drug and alcohol use, or provided and not attended. Individual barriers to accessing HCV care reported elsewhere center on perceptions that HCV is a harmless disease or knowing someone who has died of HCV, absence of symptoms, fear of liver biopsy and standard treatment side effects (such as depression, fatigue, anxiety, anemia, fatigue, nausea, insomnia and flu like symptoms, and more rarely mania, psychosis and suicide), and the hospital setting with its logistical aspects, lengthy referral and waiting times, inflexible appointment systems and limited psychosocial supports.[14,21,36,54-56] Of particular note were the significant barriers to treatment engagement reported by those with a fibroscan score of > 8.5 kPa and eligible for DAA treatment, which centered on the inability to engage with HCV treatment and care due to custodial sentencing, parental bereavement, and chaotic family and drug using lifestyles. A majority of participants in this study with fibroscan scores of > 8.5 kPa were not aware of HCV symptoms other than fatigue, and continued to struggle with drug and alcohol abuse.

Structural factors affecting access relate to stigma, social and family support, housing, income, gender and criminalization.[15] The participants in this study had very high level of unemployment (> 90%) and homelessness (40%) reflecting high levels of social deprivation and barriers that need to be addressed to improve HCV treatment uptake. These challenges underpin the clear need to continually target PWID for HCV screening and treatment, particularly using non-invasive methods such as Fibroscanning and expand methadone treatment services to include housing and employment/training interventions within community drug treatment settings.

Willingness to start HCV treatment in PWID generally ranges between 53-86%.[29, 30, 32, 57] While this study did not include data on the numbers who subsequently engaged with HCV treatment, it does show that when HCV assessment services are provided locally in community drug treatment clinics, the patients are willing and able to engage. An 80% uptake of fibro scan among this cohort is a very positive finding, particularly since over half had previously been referred and attended one hospital appointment but failed to follow up for assessment and treatment. Providing on site HCV treatment with DAAs could further impact on treatment uptake.

Assessment facilitators include becoming symptomatic, knowing HCV infection can cause liver disease and desire to be treated for this virus.[21, 36] Modifiable barriers at this individual patient level include lack of priority and knowledge, financial resources and fear of side effects [21] Zickmund and colleagues,[58] in their study of patients receiving opioid agonist therapy, described poor relations with health providers, lack of access to health care and antiviral therapies as the central barriers occurring despite intense educational efforts. Patients in this study described negative structural aspects of HCV services, which include lack of follow-up appointments and early appointments difficult to attend to due to distances, and family issues. Studies elsewhere report that patient negative views are also strongly influenced by peer networks[21] and poor mental health.[54] Peer support groups are increasingly utilized to increase engagement in the HCV cascade of care, and enhance patient knowledge.[59-60]

The barriers can be reduced by developing integrated care pathways, and incorporating HCV treatment and care within the community drug treatment services.[14, 15] Studies elsewhere emphasize the need to support and train nurses, general practitioners and addiction specialists in their key role in screening and PWID for HCV assessment and counselling.[14, 36] OST can underpin such HCV care pathways.[61] Findings from this study underpin the usefulness of provision of community fibroscanning in providing community-based treatment for "vulnerable populations" such as PWID with the new DAAs, and particularly when situated within drug treatment services. Afternoon clinics and enhanced prison referral systems are warranted.

The strengths of this study include the selection of a particularly hard to reach group of HCV chronically infected PWIDs, a cohort that need to be studied to inform how HCV assessment and treatment uptake can be improved. It is the first study in Ireland to specifically target the chronically infected PWIDs and to identify their characteristics, to assess the extent of liver disease, the numbers requiring treatment in accordance with present national HCV treatment guidelines and to explore patient identified barriers and enablers to HCV treatment. The single site location of this study reduces it generalizability.

CONCLUSION

PWID are a high-risk and high-prevalence population for HCV infection.[12, 61] Although HCV treatment is effective for PWID,[21, 62] the uptake is lower than other risk groups.[29, 63-66] Offering HCV non-invasive fibroscanning within drug treatment services can identify and target those with chronic HCV, coupled with the potential positive outcomes when engaging in OST. Self-declared HCV related symptoms are not a reliable indicator of the level of liver disease and outreach fibroscanning offers an ideal opportunity to identify patients with more advanced liver disease including cirrhosis that are eligible for DAAs. Similar barriers and enablers to HCV treatment were described by this Irish cohort of PWID as previously described in previous studies, including drug and alcohol stability, injecting drug use, fear of HCV treatment and liver biopsy, imprisonment, chaotic life style, social exclusion and stigma. Uniquely, this study found a link with methadone dose and higher fibroscan scores, a finding which requires further research. Findings are intended to inform HepCare Europe in their development of a community based model of care in order to engage with PWID who are affected and infected with HCV.

Source of Funding

The Hepcare Europe project, Co-funded by the Health Programme of the European Union, Grant agreement number 709844.

Conflict of Interest

All authors declare no conflict of interest.

REFERENCES

1. Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, *et al.* Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. Lancet 2011;378:571-83.
2. Page K, Morris MD, Hahn JA, Maher L, Prins M. Injection drug use and hepatitis C virus infection in young adult injectors: using evidence to inform comprehensive prevention. Clin Infect Dis 2013;57:S32-8.
3. Scheidell JD, Khan MR, Clifford LM, Dunne EM, Keen LD, Latimer WW. Gender differences in planning ability and hepatitis C virus among people who inject drugs. Addict Behav 2015;47:33-7.
4. Scheinmann R, Hagan H, Lelutiu-Weinberger C, Stern R, Des Jarlais DC, Flom PL, *et al.* Non-injection drug use and Hepatitis C Virus: a systematic review. Drug Alcohol Depend 2007;89:1-12.
5. Terrault NA. Sexual activity as a risk factor for hepatitis C. Hepatology 2002;36:S99-105.

6. Wiessing L, Ferri M, Grady B, Kantzanou M, Sperle I, Cullen KJ, *et al.* Hepatitis C virus infection epidemiology among people who inject drugs in Europe: a systematic review of data for scaling up treatment and prevention. PLoS One 2014;9:e103345.
7. Mohd HK, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology 2013;57:1333-42.
8. Hope VD, Eramova I, Capurro D, Donoghoe MC. Prevalence and estimation of hepatitis B and C infections in the WHO European Region: a review of data focusing on the countries outside the European Union and the European Free Trade Association. Epidemiol Infect 2014;142:270-86.
9. Lazarus JV, Sperle I, Maticic M, Wiessing L. A systematic review of Hepatitis C virus treatment uptake among people who inject drugs in the European Region. BMC Infect Dis 2014;14:S16.
10. Bostan N, Mahmood T. An overview about hepatitis C: a devastating virus. Crit Rev Microbiol 2010;36:91-133.
11. Whiteley D, Elliott L, Cunningham-Burley S, Whittaker A. Health-Related Quality of Life for individuals with hepatitis C: A narrative review. Int J Drug Policy 2015;26:936-49.
12. EMCDDA. European Drug Report 2013: Trends and development. Lisbon, Portugal; 2013.
13. Giese C, Igoe D, Gibbons Z, Hurley C, Stokes S, McNamara S, *et al.* Injection of new psychoactive substance snow blow associated with recently acquired HIV infections among homeless people who inject drugs in Dublin, Ireland, 2015. Euro Surveill 2015;20.
14. Grebely J, Bruggmann P, Treloar C, Byrne J, Rhodes T, Dore GJ, *et al.* Expanding access to prevention, care and treatment for hepatitis C virus infection among people who inject drugs. Int J Drug Policy 2015;26:893-8.
15. Harris RJ, Hope VD, Morongiu A, Hickman M, Ncube F, DE Angelis D. Spatial mapping of hepatitis C prevalence in recent injecting drug users in contact with services. Epidemiol Infect 2012;140:1054-63.
16. Lazarus JV, Shete PB, Eramova I, Merkinaite S, Matic S. HIV/hepatitis coinfection in eastern Europe and new pan-European approaches to hepatitis prevention and management. Int J Drug Policy 2007;18:426-32.
17. World Hepatitis Alliance, Viral hepatitis: Global policy, 2010, World Hepatitis Alliance. p. 1-184.
18. Wiessing L, Likatavicius G, Hedrich D, Guarita B, van de Laar MJ, Vicente J. Trends in HIV and hepatitis C virus infections among injecting drug users in Europe, 2005 to 2010. Euro Surveill. 2011;16:pii=20031. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20031
19. Linas BP, Barter DM, Leff JA, Assoumou SA, Salomon JA, Weinstein MC, *et al.* The hepatitis C cascade of care: identifying priorities to improve clinical outcomes. PLoS One 2014;9:e97317.
20. Alavi M, Raffa JD, Deans GD, Lai C, Krajden M, Dore GJ, *et al.* Continued low uptake of treatment for hepatitis C virus infection in a large community-based cohort of inner city residents. Liver Int 2014;34:1198-206.
21. Bruggmann P. Accessing Hepatitis C patients who are difficult to reach: it is time to overcome barriers. J Viral Hepat 2012;19:829-35.
22. Iversen J, Grebely J, Topp L, Wand H, Dore G, Maher L. Uptake of hepatitis C treatment among people who inject drugs attending Needle and Syringe Programs in Australia, 1999-2011. J Viral Hepat 2014;21:198-207.
23. Overbeck K, Bruggmann P, Helbling B. Chronic Hepatitis C virus infection in Swiss primary care practices: low case loads-high barriers to treatment? Eur J Gen Pract 2011;17:103-8.
24. Martin NK, Vickerman P, Miners A, Foster GR, Hutchinson SJ, Goldberg DJ, *et al.* Cost-effectiveness of hepatitis C virus antiviral treatment for injection drug user populations. Hepatology 2012;55:49-57.
25. Martin NK, Pitcher AB, Vickerman P, Vassall A, Hickman M. Optimal control of hepatitis C antiviral treatment programme delivery for prevention amongst a population of injecting drug users. PLoS One 2011;6:e22309.
26. Aspinall EJ, Corson S, Doyle JS, Grebely J, Hutchinson SJ, Dore GJ, *et al.* Treatment of hepatitis C virus infection among people who are actively injecting drugs: a systematic review and meta-analysis. Clin Infect Dis 2013;57:S80-9.
27. Hellard ME, Wang YH. The role of general practitioners in managing and treating hepatitis C. Med J Aust 2009;191:523-4.
28. Canfield KM, Smyth E, Batki SL. Methadone maintenance patients' knowledge, attitudes, beliefs, and experiences concerning treatment for hepatitis C virus infection. Subst Use Misuse 2010;45:496-514.
29. Grebely J, Genoway KA, Raffa JD, Dhadwal G, Rajan T, Showler G, *et al.* Barriers associated with the treatment of hepatitis C virus infection among illicit drug users. Drug Alcohol Depend 2008;93:141-7.
30. Strathdee SA, Latka M, Campbell J, O'Driscoll PT, Golub ET, Kapadia F, *et al.* Factors associated with interest in initiating treatment for hepatitis C Virus (HCV) infection among young HCV-infected injection drug users. Clin Infect Dis 2005;40:S304-12.
31. Treloar C, Holt M. Drug treatment clients' readiness for hepatitis C treatment: implications for expanding treatment services in drug and alcohol settings. Aust Health Rev 2008;32:570-6.
32. Walley AY, White MC, Kushel MB, Song YS, Tulsky JP. Knowledge of and interest in hepatitis C treatment at a methadone clinic. J Subst Abuse Treat 2005;28:181-7.
33. Ghany MG, Strader DB, Thomas DL, Seeff LB. Diagnosis, management, and treatment of hepatitis C: an update. Hepatology 2009;49:1335-74.
34. Huang R, Jiang N, Yang R, Geng X, Lin J, Xu G, *et al.* Fibroscan improves the diagnosis sensitivity of liver fibrosis in patients with chronic hepatitis B. ExpTher Med 2016;11:1673-7.
35. Sharma P, Dhawan S, Bansal R, Tyagi P, Bansal N, Singla V, *et al.* Usefulness of transient elastography by FibroScan for the evaluation of liver fibrosis. Indian J Gastroenterol 2014;33:445-51.
36. Swan D, Long J, Carr O, Flanagan J, Irish H, Keating S, *et al.* Barriers to and facilitators of hepatitis C testing, management, and treatment among current and former injecting drug users: a qualitative exploration. AIDS Patient Care STDS 2010;24:753-62.
37. Arain A, De Sousa J, Corten K, Verrando R, Thijs H, Mathei C, *et al.* Pilot Study: Combining Formal and Peer Education with FibroScan to Increase HCV Screening and Treatment in Persons who use Drugs. J Subst Abuse Treat 2016;67:44-9.
38. Arora S, Kalishman S, Dion D, Som D, Thornton K, Bankhurst A, *et al.* Partnering urban academic medical centers and rural primary care clinicians to provide complex chronic disease care. Health Aff (Millwood) 2011;30:1176-84.
39. Foucher J, Reiller B, Jullien V, Léal F, di Cesare ES, Merrouche W, *et al.* FibroScan used in street-based outreach for drug users is useful for hepatitis C virus screening and management: a prospective study. J Viral Hepat 2009;16:121-31.
40. Marshall AD, Micallef M, Erratt A, Telenta J, Treloar C, Everingham H, *et al.* Liver disease knowledge and acceptability of non-invasive liver fibrosis assessment among people who inject drugs in the drug and alcohol setting: The LiveRLife Study. Int J Drug Policy 2015;26:984-91.
41. Moessner BK, Jørgensen TR, Skamling M, Vyberg M, Junker P, Pedersen C, *et al.* Outreach screening of drug users for cirrhosis with transient elastography. Addiction 2011;106:970-6.
42. Thornton L, Murphy N, Jones L, Connell J, Dooley S, Gavin S, *et al.* Determination of the burden of hepatitis C virus infection in Ireland. Epidemiol Infect 2012;140:1461-8.
43. Grogan L, Tiernan M, Geogeghan N, Smyth B, Keenan E. Bloodborne virus infections among drug users in Ireland: a retrospective cross-sectional survey of screening, prevalence, incidence and hepatitis B immunisation uptake. Ir J Med Sci 2005; 174: 14-20.
44. Keating S, Coughlan S, Connell J, Sweeney B, Keenan E. Hepatitis C viral clearance in an intravenous drug-using cohort in the Dublin area. Ir J Med Sci 2005;174:37-41.

45. Allwright S, Bradley F, Long J, Barry J, Thornton L, Parry JV. Prevalence of antibodies to hepatitis B, hepatitis C, and HIV and risk factors in Irish prisoners: results of a national cross sectional survey. BMJ 2000;321:78-82
46. Healy CM, Cafferkey MT, Conroy A, Dooley S, Hall WW, Beckett M, *et al.* Hepatitis C infection in an Irish antenatal population. Ir J Med Sci 2000;169:180-2.
47. Long J, Allwright S, Barry J, Reynolds SR, Thornton L, Bradley F, *et al.* Prevalence of antibodies to hepatitis B, hepatitis C, and HIV and risk factors in entrants to Irish prisons: a national cross sectional survey. BMJ 2001;323:1209-13.
48. Smyth BP, Barry J, Keenan E. Irish injecting drug users and hepatitis C: the importance of the social context of injecting. Int J Epidemiol 2005;34:166-72
49. Smyth BP, Keenan E, O'Connor JJ. Bloodborne viral infection in Irish injecting drug users. Addiction 1998;93:1649-56.
50. Long J, Keenan E, Grogan L, Mullen L, Barry J, Sinclair H. HIV infection among heroin users and area of residence. Ir Med J 2006;99:230-3.
51. Carew A M, Murphy N, Long J, Hunter K, Lyons S, Walsh C, Thornton L Hepatology, Medicine and Policy. 2017 Jan 26;2(1):7
52. O'Connell T, Thornton L, O'Flanagan D, Staines A, Connell J, Dooley S, *et al.* Prevalence of hepatitis B anti-core antibody in the Republic of Ireland. Epidemiol infect 2000;125:701-4.
53. Long J, Allwright S, Begley C. Fear and denial: how prisoners cope with risk of or diagnosis with hepatitis C. Ir J Med Sci 2003;172.
54. Evon DM, Simpson KM, Esserman D, Verma A, Smith S, Fried MW. Barriers to accessing care in patients with chronic hepatitis C: the impact of depression. Aliment Pharmacol Ther2010;32:1163-73.
55. McGowan CE, Fried MW. Barriers to hepatitis C treatment. Liver Int 2012;32:151-6.
56. Cullen W, Kelly Y, Stanley J, Langton D, Bury G. Experience of hepatitis C among current or former heroin users attending general practice. Ir Med J 2005 Mar;98:73-4.
57. Doab A, Treloar C, Dore GJ. Knowledge and attitudes about treatment for hepatitis C virus infection and barriers to treatment among current injection drug users in Australia. Clin Infect Dis 2005;40:S313-20.
58. Zickmund SL, Campbell SA, Tirado CF, Zook CL, Weinrieb RM. Perceived barriers to hepatitis C therapy for patients receiving opioid agonist treatment. J Addict Med 2012;6:233-9.
59. Grebely J, Petoumenos K, Matthews GV, Haber P, Marks P, Lloyd AR, *et al.* Factors associated with uptake of treatment for recent hepatitis C virus infection in a predominantly injecting drug user cohort: The ATAHC Study. Drug Alcohol Depend 2010;107:244-9.
60. Sylvestre DL, Clements BJ. Adherence to hepatitis C treatment in recovering heroin users maintained on methadone. Eur J Gastroenterol Hepatol 2007;19:741-7.
61. Perlman DC, Jordan AE, Uuskula A, Huong DT, Masson CL, Schackman BR, *et al.* An international perspective on using opioid substitution treatment to improve hepatitis C prevention and care for people who inject drugs: Structural barriers and public health potential. Int J Drug Policy 2015;26:1056-63.
62. Zanini B, Lanzini A. Antiviral treatment for chronic hepatitis C in illicit drug users: a systematic review. AntivirTher 2009;14:467-79.
63. Mehta SH, Genberg BL, Astemborski J, Kavasery R, Kirk GD, Vlahov D, *et al.* Limited uptake of hepatitis C treatment among injection drug users. J Community Health 2008;33:126-33.
64. Schaefer M, Hinzpeter A, Mohmand A, Janssen G, Pich M, Schwaiger M, *et al.* Hepatitis C treatment in "difficult-to-treat" psychiatric patients with pegylated interferon-alpha and ribavirin: response and psychiatric side effects. Hepatology 2007;46:991-8.
65. Grebely J, Raffa JD, Lai C, Krajden M, Kerr T, Fischer B, *et al.* Low uptake of treatment for hepatitis C virus infection in a large community-based study of inner city residents. J Viral Hepat 2009;16:352-8.
66. Grebely J, Knight E, Genoway KA, Viljoen M, Khara M, Elliott D, *et al.* Optimizing assessment and treatment for hepatitis C virus infection in illicit drug users: a novel model incorporating multidisciplinary care and peer support. Eur J Gastroenterol Hepatol 2010;22:270-7.

How to cite this article: Crowley D, Cullen W, Laird E, Lambert JS, Mc Hugh T, Murphy C, *et al.* Exploring patient characteristics and barriers to Hepatitis C treatment in patients on opioid substitution treatment attending a community based fibro-scanning clinic. J Transl Intern Med 2017; 5: 112-119.