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*Published in:*
Journal of Viral Hepatitis

*DOI:*
10.1111/jvh.13035

*Publication date:*
2018

*Document Version*
Publisher's PDF, also known as Version of record

Received: 11 September 2018 | Accepted: 11 October 2018

DOI: 10.1111/jvh.13035



ORIGINAL ARTICLE

WILEY JOURNAL OF VIRAL HEPATITIS JVH

# High response and re-infection rates among people who inject drugs treated for hepatitis C in a community needle and syringe programme

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**Funding information**
F. Hoffmann-La Roche; Scottish Government, Department Public Health; Janssen Pharmaceuticals; NIHR HPRU EI

## Summary

To achieve WHO hepatitis C virus (HCV) elimination targets by 2030, mathematical models suggest there needs to be significant scale-up of treatment among people who inject drugs (PWID). We tested whether people who actively inject drugs can be recruited and treated successfully through a community needle and syringe programme (NSP), and assessed rates of re-infection. 105 HCV RNA positive participants were enrolled prospectively. Participants were recruited from the largest NSP in Dundee over 42 months. 94/105 individuals commenced treatment. Genotype 1 (G1) individuals (n = 37) were treated with peg-interferon+ribavirin+Simepravir/Telaprevir. Genotype 2/3 (G2/3) (n = 57) received peg-interferon+ribavirin. Weekly study visits took place within the NSP. Mean age of participants was 34.0 years (SD 6.9), 71.3% (61/94) were male. One in five (20/94) participants were homeless. 68.1% (64/94) were on OST (opiate substitution therapy) at enrolment; participants injected median 6.5 times/wk. In terms of clinical outcomes, >80% treatment adherence was 71.3% (67/94). There was no difference in SVR-12 rates by genotype: 81.0% (30/37) for G1 and 82.5% (47/55) for G2/3. At 18 months post-treatment, 15/77 participants were reinfected, followed up over 69.8 person-years, yielding a re-infection rate of 21.5/100 person-years (95% CI 13.00-35.65). This trial demonstrates that HCV treatment can be delivered successfully to the target population of treatment as prevention strategies. We report higher rates of re-infection than existing estimates among PWID. Scale-up of HCV treatment should be pursued alongside a comprehensive programme of harm reduction interventions to help minimize re-infection and reduce HCV transmission.

**KEYWORDS**
hepatitis C virus, injecting drug use, people who inject drugs, re-infection, treatment as prevention

**Abbreviations:** BBV, blood-borne viruses; DAA, direct-acting antivirals; DBS, dried blood spot; HCV, hepatitis C virus; IDU, injecting drug use; NSP, Needle and Syringe Programmes; OST, opioid substitution therapy; PWID, people who inject drugs.

## 1 | INTRODUCTION

The global burden of hepatitis C virus (HCV)-related liver disease continues to rise.[1] In 2010, the number of deaths due to HCV was estimated to be 500 000 worldwide.[2] WHO targets are to eliminate HCV by 2030.[3] In Scotland, over 90% of new HCV infections occur among people who inject drugs (PWID).[4] HCV antibody prevalence among PWID is 58%, similar to other European countries.[5,6]

In 2016, 1.76 million of the 71 million people living with HCV worldwide received treatment (~2.48% treatment uptake).[7] Treatment uptake has been historically low among PWID prior to the introduction of new direct-acting antivirals (DAA) treatments.[8] However, there is now good evidence that HCV treatment is safe and effective among PWID.[9-12] The latest international guidelines[13,14] now recommend treatment for all PWID. However, latest data from Hep-CORE study found 8/25 (32%) of European countries surveyed continue to refuse treatment to PWID.[15]

Treating active PWID also has the potential to reduce HCV transmission, a concept known as treatment as prevention (TasP). Modelling data suggest that scaling-up treatment among current PWID with DAAs is critical to reducing HCV prevalence,[16-18] and is

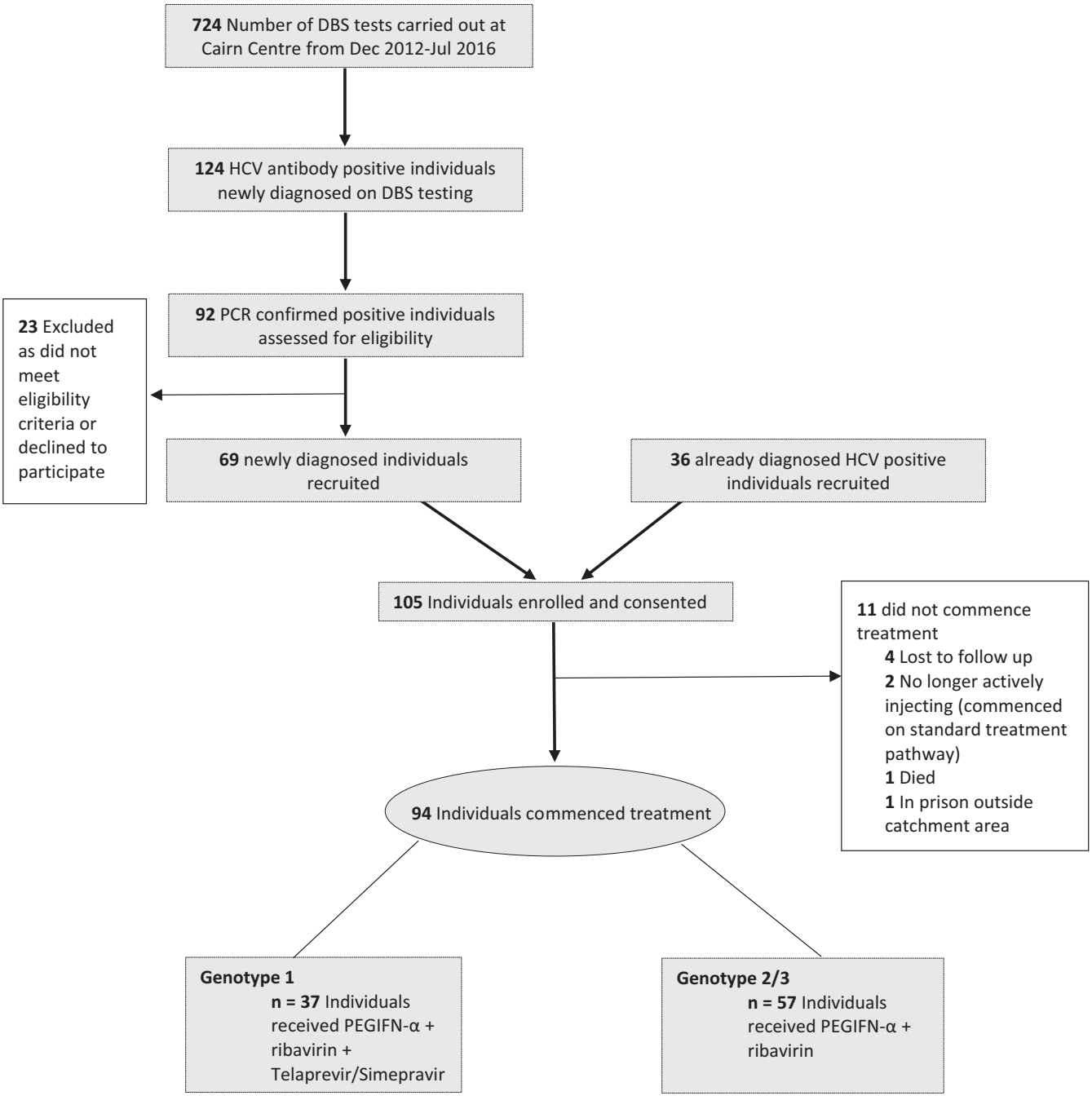


**FIGURE 1** Flow diagram of cohort recruitment into Eradicate study

cost-effective in settings such as the UK with moderate HCV prevalence.[19] Reductions in prevalence are greater when combined with scale-up of harm reduction interventions—opioid substitution therapy (OST) and high coverage Needle and Syringe Programmes (NSP).[20-22] Recent modelling of the Scottish epidemic attributed 55% of the reduction in HCV incidence from 14.2/100 pyrs in 2008 to 5.5/100 in 2015 to national scale-up of harm reduction interventions.[21]

To date, studies assessing HCV treatment success among PWID have recruited from populations engaged in hepatology or specialist addiction services.[9,10,23,24] These studies define "active injecting drug use" as those who have injected in the last 6 or 12 months, and many require a period of abstinence from injecting drug use (IDU) prior to starting treatment. These are therefore populations of largely stable PWID, at low risk of transmitting HCV. To achieve the greatest reduction in HCV incidence, treatment programmes should target PWID who are most likely to transmit the virus. This is the study population we aimed to recruit.

In this study, we aimed to test whether 100 people who were currently injecting drugs could be recruited and successfully treated for HCV in a NSP. We also assessed rates of re-infection. The secondary aims were to identify factors associated with treatment adherence, re-infection and cure.

## 2 | METHODS

### 2.1 | Study design and cohort recruitment

Eradicate was a prospective observational study conducted at the largest Needle and Syringe Programme (NSP) in Dundee, Scotland. Participants were recruited between December 2012 and July 2016 (Figure 1). Since 2009, all PWID attending the central NSP in Dundee (range 1280-2118 anonymous individuals per year between 2012 and 2016) were offered yearly dried blood spot testing (DBS) for blood-borne viruses (BBV) (range 123-203 identified PWID tested per year 2009-2016). During the study enrolment period, all PWID who tested positive for HCV and fulfilled study enrolment criteria (Table 1) were invited to participate. Only individuals who had injected in the past week were eligible for the study. Recruitment was carried out by on-site research nurses. All participants who were not already prescribed OST were offered low-threshold methadone treatment at enrolment. This was defined as low-threshold as the primary goal was improved HCV treatment adherence, not complete abstinence.[25] Each participant was offered naloxone training, as recommended by clinical guidelines.[26] All participants provided written informed consent. Ethical approval was obtained from the East of Scotland Research Ethics committee.

### 2.2 | HCV treatment

HCV treatment followed standard NHS clinical practice at the time of study enrolment. Individuals were treated with peg-interferon+ribavirin+/− protease inhibitor for 12, 16 or 24 weeks (see Appendix S1). During treatment, patients attended weekly study visits at the NSP. At each weekly visit, participants received an interferon injection and a week's supply of tablets. Participants who were subsequently in prison had medication delivered weekly.

**TABLE 1** Inclusion and exclusion criteria for Eradicate study

| |
|---|
| **Inclusion criteria** |
| 1. Age 18-70 y |
| 2. Active HCV positive infection confirmed with PCR |
| 3. Current injecting drug use established through review of needle injection sites and patient history |
| 4. If female, negative urine test for pregnancy and on Long-Acting Reversible Contraception during study |
| **Exclusion criteria** |
| 1. Aggressive or violent behaviour |
| 2. Features of decompensated liver failure |
| 3. Evidence of primary hepatocellular carcinoma |
| 4. Pregnancy, breastfeeding or pre-menopausal female not using effective contraception |
| 5. Contraindications to peg-interferon or Ribavirin |
| 6. Previous treatment with peg-interferon and Ribavirin |
| 7. Participation in a drug study within previous 30 d |
| 8. Inability to provide informed consent |

### 2.3 | Data collection

At enrolment (visit 1), participants completed a questionnaire comprising of: demographics; social history (current living situation, employment, incarceration); medical and psychiatric history; alcohol and drug use; and injecting practices. Baseline bloods including viral load, genotyping, HIV, hepatitis B, full blood count, ferritin, urea & electrolytes, liver function tests were obtained and level of fibrosis level was assessed using Fibroscan or Fib4 scores. At visit 2, participants commenced treatment.

Prior to treatment commencement participants completed the EuroQol-5 Dimensions questionnaire (EQ-5D-3L).[27] Participants were assessed weekly for adverse events, which were managed as per local standard clinical practice. At each visit, participants were given a £5 supermarket voucher (contingency management) and week supply of protein drinks. Monitoring bloods were taken weekly for the first four weeks, then fortnightly until end of treatment. HCV RNA was obtained at week 4 (to determine rapid virological response), week 12 and end of treatment. Participants were PCR tested post-treatment to determine sustained virological response at 12 weeks (SVR-12), and at 6- and 18-month post-treatment to determine re-infection.

### 2.4 | Study outcomes and analysis

Three primary outcomes were assessed: (a) successful recruitment of our target population into the study; (b) proportion who achieved SVR-12; (c) re-infection rate. All positive post-treatment PCR RNA

results were genotyped to determine whether this represented a new HCV strain. Re-infection was defined as a positive PCR result at 6- or 18-month post-treatment, for individuals who achieved SVR-12. The secondary outcome was treatment adherence. Adherence was defined using the "80/80/80 rule": participants must complete 80% interferon injections and 80% ribavirin tablets for 80% of the treatment duration. At each study visit, patients returned any unused tablets from the previous week to estimate weekly medication compliance.

#### 2.4.1 | EQ5D

The EQ5D-5D-3L is a standardized questionnaire which assesses quality of life (QoL) in five dimensions. It is widely used to measure health states among this population.[28,29] During analysis, a single summary QoL index value for each participant was derived using country-specific EQ-5D value sets and a known algorithm.[30] These were then compared to latest UK population norms by age and sex.[31]

#### 2.4.2 | SVR and adherence

Univariable logistic regression was performed to determine factors associated with treatment adherence. Predictor variables decided a priori[23,32] included age, sex, on OST treatment, length HCV treatment, incarceration during treatment, homelessness, living with other PWID, history of anxiety and depression and injecting frequency. Logistic regression was also used to assess predictors of SVR-12. Factors were based on known predictors of SVR-12 from existing literature.[23,32-34] These included treatment adherence, age, sex, fibrosis score, HCV genotype and pre-treatment HCV RNA level. We hypothesized that OST treatment, homelessness, incarceration, living with other PWID, history of anxiety and depression and injecting frequency may also be associated with attainment of SVR-12. However, any association would be mediated through their impact on adherence; therefore, they were not included in the SVR-12 logistic regression analysis.

#### 2.4.3 | Re-infection rate

The incidence of re-infection is expressed in person-years. Time at risk began following attainment of SVR-12 and ended at date of re-infection or date of last negative PCR test (if not reinfected). The time at which re-infection occurred was estimated to be the mid-point between the last negative and first positive PCR result. One participant had become reinfected at 3 months (PCR negative at end of treatment, PCR positive at 3 months with different genotype). For this participant, the time-at-risk period was the mid-point between end-of-treatment and SVR-12. Participants who did not achieve SVR-12 or who died prior to 6-month PCR test were excluded from estimates of re-infection. Participants who were lost to follow-up were censored at the last post-treatment PCR test obtained. Six patients were not yet 18-month post-treatment and were therefore censored at 6 months.

Poisson regression assessed factors associated with re-infection rate. These included age, sex, on OST treatment, homelessness, living with other PWID, history of anxiety and depression and injecting frequency.[35,36] All analysis was performed in STATA.

## 3 | RESULTS

### 3.1 | Recruitment and baseline characteristics

A total of 724 individuals were tested for HCV at the Needle and Syringe Programme (NSP) during study enrolment period (Figure 1). Of these, 145/724 (20.0%) were HCV antibody positive on DBS testing, with 92 positive on PCR RNA testing. Of these newly diagnosed individuals, 69/92 were recruited into the study. 36 individuals already known to be positive from previous testing were also recruited. This gives a total of 105 individuals were enrolled into the study, with 94 participants ultimately commencing treatment (Figure 1).

For participants commencing treatment (n = 94), mean age was 34 (SD 6.9) years; the majority, 71.3% (67/94), were male; 1 in 5 participants were homeless or living in unstable accommodation (20/94); and 12.8% (12/94) were in prison at some point during the treatment period (Table 2). Reported history of anxiety/depression was high, 69.2% (65/94), and 37/94 (39.4%) reported a previous suicide attempt. Median injecting frequency was 6.5 times/week; 54.3% (51/93) participants injected daily/more than once a day. Reported alcohol consumption was comparatively low: 9.6% (9/94) consumed alcohol >3 times a week.

Median health utility was 0.72 (IQR 0.41-0.85) on EQ5D, with nearly ¾ (74%) of the study population reporting a health utility below the 25th percentile, when compared to the general UK population of a similar age and sex.[31] In terms of harm reduction interventions; the majority, 82.4% (75/91), had 100% needle and syringe provision (1 or more needles obtained from NSP for each injection reported),[37] and 62.5% (55/88) were receiving opiate substitution therapy (OST) prior to enrolment (with a further 11 participants commenced on OST at enrolment). 39.4% (37/94) were genotype 1 (G1), 60.6% (57/94) genotype 2/3 (G2/3). Levels of significant fibrosis (F2-F4) were low; 17/94 (18.1%). All participants were HIV and hepatitis B negative.

### 3.2 | Treatment outcomes

Overall, 82% (77/94) participants achieved SVR-12 (Appendix S2). There was no difference in SVR12 rates between genotype: 81.0% (30/37) for G1 and 82.5% (47/57) for G2/3. 71.3% (67/94) individuals achieved ≥80% treatment adherence (Table 3). Reasons for non-adherence are available for 15/27 participants; eight missed multiple appointments, four were admitted to hospital with injecting-related health problems and advised to stop treatment; two withdrew from treatment due to deteriorating mental health; one died from suspected drug overdose. Of the 64/94 participants on OST at enrolment, the majority, 93.8% (60/64), remained on OST during the treatment period. All participants attended follow-up at 6-month

**TABLE 2** Baseline characteristics of study population

| Characteristic | n = 94 | % |
|---|---|---|
| Demographics | | |
| Age, mean (SD) (range), years | 34.0 (6.9) (21-49) | |
| Male | 67 | 71.3 |
| Living situation and employment | | |
| Owned or rented housing | 67 | 71.3 |
| Homeless/unstable housing[a] | 20 | 21.3 |
| Living with other PWID | 34 | 37.0 |
| Unemployed | 88 | 93.6 |
| Incarceration[b] | 12 | 12.8 |
| Current drug and alcohol use | | |
| Opiates | 93 | 98.9 |
| Benzodiazepines | 55 | 58.5 |
| Legal highs | 13 | 13.8 |
| Gabapentin/Pregabalin | 38 | 40.4 |
| Cannabis | 57 | 60.6 |
| Amphetamines | 5 | 5.3 |
| Consume alcohol >3 time a week | 9 | 9.6 |
| Injecting practices | | |
| No. years injecting[c], mean (SD) (IQR) | 9.7 (7.0) (5-13) | |
| No. times injected in past week[d], median (SD) (IQR) | 6.5 (9.3) (2-14) | |
| Inject daily/more than once a day[d,e] | 51 | 54.3 |
| No. clean needles obtained per week[f] median (SD) (IQR) | 10 (19.2) (5-20) | |
| Harm reduction coverage | | |
| 100% needle and syringe provision[f,g] | 75 | 82.4 |
| On OST prior to enrolment[h] | 55 | 62.5 |
| Mental and social health | | |
| EQ5D health utility, median (IQR) | 0.72 (0.41-0.85) | |
| History anxiety/Depression | 65 | 69.2 |
| Previous suicide attempt | 37 | 39.4 |
| Clinical measures | | |
| HCV Genotype | | |
| 1 | 37 | 39.4 |
| 2/3 | 57 | 60.6 |
| Significant fibrosis (F2-F4)[i] | 17 | 18.1 |
| HCV RNA (IU/mL), median (IQR) | 440 000 (61 000, 1 700 000) | |

[a]Temporary/unstable accommodation/hostel/sofa surfing.
[b]In prison for part or all of treatment period.
[c]Four participants did not wish to answer (n = 90).
[d]One participant did not wish to answer (n = 93).
[e]During an average month of injecting.
[f]Three participants did not wish to answer (n = 91).
[g]One or more needles obtained from a needle exchange centre for each injection reported.
[h]Missing data for six participants (n = 88).
[i]Using baseline Fibroscan scores or FIB-4 index for patients who did not have Fibroscan results.

post-treatment. At 18 months, nine participants had been lost to follow-up (Figure 2).

In total, eight participants had died by 18-month follow-up. Cause of death is available in 5/8 cases; four participants died from suspected drug overdose, one participant died of septicaemia secondary to injection of drugs. This gives an overall mortality rate of 5.55/100 person-years (95% CI 2.77-11.09) during treatment and follow-up period (total follow-up time 144.24 years).

### 3.3 | Predictors of treatment adherence and SVR-12

Longer treatment length (24 weeks vs 12/16 weeks) was associated with reduced treatment adherence, OR 0.35 (95% CI 0.13-0.98) ($P = 0.047$) (Table 4). Remaining on OST during the study was weakly associated with increased adherence, OR 2.03 (95% CI 0.82-5.08) ($P = 0.13$). There was no convincing evidence of an association between adherence and other hypothesized factors; age, sex, unstable housing, incarceration, living with other drug users, injecting frequency, history anxiety/depression. Therefore, multivariable analysis was not performed.

In univariable analysis, a greater proportion of treatment adherent participants achieved SVR (OR 7.00, 95% CI 2.24-21.8, $P < 0.001$) (Appendix S3). Age, sex, fibrosis level, PCR RNA level and genotype did not independently predict achievement of SVR-12. In adjusted analysis, with all variables from unadjusted analysis included in model, adherence remained positively correlated with achieving SVR ($P < 0.001$).

### 3.4 | Re-infection rate

At six months, 5/77 participants who achieved SVR-12 had become reinfected yielding a re-infection rate of 23.53/100 person-years (95% CI 9.80-56.54). The total follow-up time was 21.25 person-years. At 18 months, there were 15/77 re-infections giving a cumulative 18-month re-infection rate of 21.49/100 person-years (95% CI 13.00-35.65) over total follow-up time 69.79 person-years.

Unadjusted analysis found age <30 years was weakly associated with a higher re-infection rate (vs 30-40 years, $P = 0.063$) (vs >40 years, $P = 0.14$). There was no evidence of correlation between other hypothesized factors (Table 4). Therefore, we did not perform multivariable regression.

## 4 | DISCUSSION

### 4.1 | Main findings

We show that it is feasible to recruit people who inject drugs (PWID) from a community-based needle and syringe programme (NSP) onto HCV treatment, and achieve over 80% SVR-12 and impressive treatment adherence (even with older regimens). Re-infection rates, however, in this population were high at 21.5/100 person-years (95% CI

13.00-35.65) at 18-month post-treatment. Mortality rates in our population also were high.

## 4.2 | Strengths and limitations

This is the first HCV treatment study, to our knowledge, in which all enrolment, treatment and follow-up took place in the community at a Needle and Syringe Programme (NSP) and that active injecting was an inclusion criteria. This model achieved high levels of HCV testing and treatment uptake among active injectors, with very low loss to follow-up. The study population is unique; at enrolment, all participants had injected within the past week representing a highly active population of injectors.

The study has several limitations. First, it was a small-scale pilot study involving 94 participants, based in one NSP in Dundee. The size of the study meant there was insufficient power to identify independent predictors of adherence, SVR-12 and re-infection. Injecting risk patterns following SVR-12 were unavailable which also limited analysis of predictors of re-infection. Second, recruitment began before the shift in clinical practice from interferon-based treatment to DAAs—though even with older regimens very high rates of SVR-12 were achieved. We expect that higher rates of cure should be possible with more effective, better tolerated DAAs. Third, follow-up positive PCR results were genotyped to distinguish between relapse and re-infection. Gold standard would be sequencing to confirm re-infection.

**TABLE 3** HCV treatment adherence, sustained viral response, re-infection and deaths

| Genotype | G1 | | G2/3 | | Total | |
|---|---|---|---|---|---|---|
| **Study outcome** | **N** | **%** | **n** | **%** | **n** | **%** |
| Genotype | 37 | 39.4 | 57 | 60.6 | 94 | 100 |
| SVR-12[a] | 30 | 81.0 | 47 | 82.5 | 77 | 81.9 |
| ≥80% treatment adherence | | | | | 67 | 71.3 |
| Re-infections at 6 mo[b] | | | | | 5 | |
| Re-infections at 18 mo[b] | | | | | 15 | |
| Deaths at 6 mo | | | | | 3 | |
| Deaths at 18 mo | | | | | 8 | |

[a]SVR-12: sustained virological response at 12 wk.
[b]Cumulative number of re-infections.

## 4.3 | Comparison to existing literature and implications

This study reports rates of re-infection following treatment that are significantly higher than existing estimates among PWID. Two meta-analyses estimate a pooled re-infection rate among PWID of

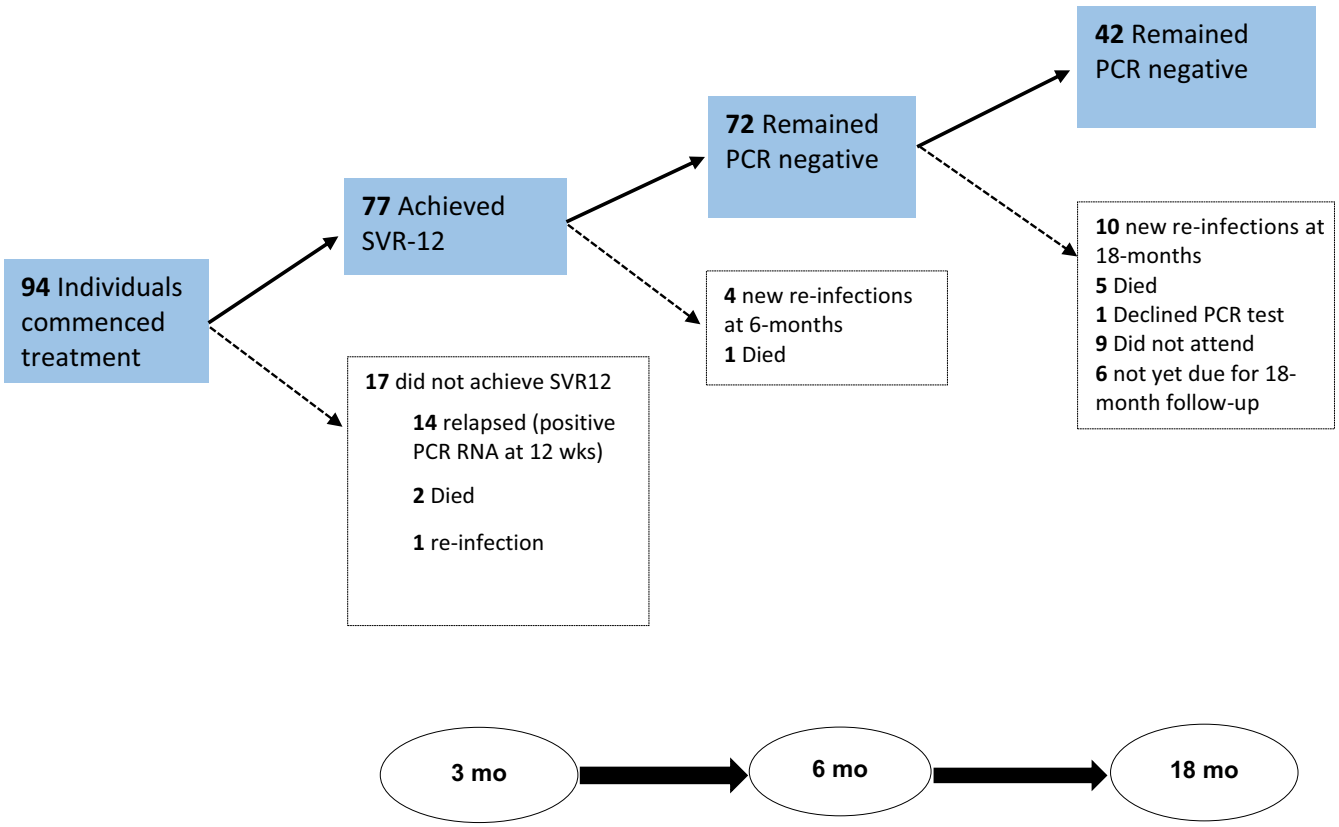


**FIGURE 2** Flow diagram of study outcomes at 3-mo, 6-mo and 18-mo follow-up

**TABLE 4** Univariable analysis of factors predicted to be associated with treatment adherence and re-infection rate

| | ≥80% Treatment adherence | | | | | 18-mo Re-infection rate | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Factor | ≥80% adherence (n = 67) | Total (n = 94) | % | OR (95% CI) | *P*-value | Re-infections (n = 15) | Total (n = 78) | % | Re-infection rate ratio (95% CI) | *P*-value |
| Age | | | | | | | | | | |
| <30 | 22 | 29 | 75.9 | 1.00 | | 9 | 26 | 34.6 | 1.00 | |
| 30-40 | 32 | 45 | 71.1 | 0.78 (0.27-2.28) | 0.65 | 5 | 38 | 13.2 | 0.35 (0.12-1.06) | 0.063 |
| >40 | 13 | 20 | 65.0 | 0.59 (0.17-2.07) | 0.41 | 1 | 14 | 7.1 | 0.21 (0.026-1.65) | 0.14 |
| Sex | | | | | | | | | | |
| Male | 48 | 67 | 71.6 | 1.00 | | 11 | 56 | 19.6 | 1.00 | |
| Female | 19 | 27 | 70.4 | 0.94 (0.35-2.51) | 0.90 | 4 | 22 | 18.2 | 0.83 (0.26-2.60) | 0.74 |
| Opiate substitution therapy[a] | | | | | | | | | | |
| Stopped/never started | 21 | 34 | 61.8 | 1.00 | | 6 | 22 | 27.3 | 1.00 | |
| Remained on OST during treatment | 46 | 60 | 76.7 | 2.03 (0.82-5.08) | 0.13 | 9 | 56 | 16.1 | 0.59 (0.21-1.65) | 0.31 |
| Treatment length | | | | | | | | | | |
| 12/16 wk | 30 | 36 | 83.3 | 1.00 | | | | | | |
| 24 wk | 37 | 58 | 63.8 | 0.35 (0.13-0.98) | 0.047 | | | | | |
| Homeless/unstable housing | | | | | | | | | | |
| No | 53 | 74 | 71.6 | 1.00 | | 14 | 65 | 21.5 | 1.00 | |
| Yes | 14 | 20 | 70.0 | 0.93 (0.31-2.73) | 0.89 | 1 | 13 | 7.7 | 0.42 (0.056-3.23) | 0.39 |
| Incarceration[b] | | | | | | | | | | |
| No | 56 | 82 | 68.3 | 1.00 | | | | | | |
| Yes | 11 | 12 | 91.7 | 5.11 (0.63-41.68) | 0.13 | | | | | |
| Living with other people who inject drugs[c] | | | | | | | | | | |
| No | 42 | 57 | 73.7 | 1.00 | | 9 | 49 | 18.4 | 1.00 | |
| Yes | 22 | 34 | 64.7 | 0.66 (0.26-1.64) | 0.37 | 6 | 27 | 22.2 | 1.10 (0.39-3.10) | 0.85 |
| Legal high use | | | | | | | | | | |
| No | 60 | 81 | 74.1 | 1.00 | | 13 | 68 | 19.1 | 1.00 | |
| Yes | 7 | 13 | 53.9 | 0.41 (0.12-1.35) | 0.14 | 2 | 10 | 20.0 | 1.02 (0.23-4.51) | 0.98 |
| Injecting ≥ daily[d] | | | | | | | | | | |
| No | 31 | 42 | 73.8 | 1.00 | | 8 | 39 | 20.5 | 1.00 | |
| Yes | 35 | 51 | 68.6 | 0.78 (0.31-1.92) | 0.58 | 7 | 38 | 18.4 | 0.84 (0.31-2.32) | 0.74 |
| History anxiety/depression | | | | | | | | | | |
| No | 22 | 29 | 75.9 | 1.00 | | 6 | 24 | 25.0 | 1.00 | |
| Yes | 45 | 65 | 69.2 | 0.57 (0.19-1.74) | 0.33 | 9 | 54 | 16.7 | 0.57 (0.20-1.60) | 0.28 |

[a]Missing data for six participants (n = 88).
[b]In prison for part or all of treatment period.
[c]Three participants did not wish to answer (n = 91).
[d]One participant did not wish to answer (n = 93).

1.77/100 pyrs to 2.4/100 pyrs.[10,38] Though recent studies report greater re-infection rates among higher risk populations; 4.9/100 person-years among relapsed PWID[39] to 5.7/100 person-years among individuals hospitalized for a drug-related cause.[35] However, all these studies[10,35,36,38-43] defined "active PWID" as those who have "injected in the past 6- or 12-months"—except Hilsden et al[44] who defined "active" as having injected in the past 3 months, with a reported re-infection rate of 2.8/100 person-years. This is significantly different to our study population, all of whom had injected in the past week and the majority were injecting daily.

In fact, these re-infection rates are closer to latest estimates of HCV incidence among recent injectors (past 6 months) in Scotland at 12.4/100 pyrs (CI 6.8-19.5) in 2015/2016.[45] This has two implications. First, the evidence supports a critical assumption of impact and economic models that there may be no additional behaviour change following HCV treatment (over and above exposure to other interventions) and re-infection rates are similar to HCV incidence in the community.[16,17,19] Second, the high HCV incidence and re-infection rates highlight the failure of current coverage and intensity of harm reduction interventions to minimize injecting risk.

This high re-infection rate, along with a significant mortality rate (5.55/100 person-years) and high level of incarceration (12.8% in prison at some point during study period), indicate this is an unstable population who would benefit from a broader programme of social and psychological interventions—alongside NSP and OST provision—to reduce injecting risk, as recommended by recent UK clinical guidelines.[26] Once treated, at-risk individuals should continue to be regularly tested for re-infection and retreated if active infection is detected, as per latest international guidelines.[14] At the time of writing this paper, 10/15 of reinfected participants are currently being retreated or have completed retreatment.

SVR-12 rates are higher than reported rates among PWID for these drugs in the literature.[10,32] This may be due to several factors. The study population is on average younger, with lower fibrosis scores and lower initial HCV RNA levels compared to those in existing studies.[10,32] These are well-described factors associated with higher cures for interferon, ribavirin and first-generation protease inhibitors. Health-related quality of life was low, in keeping with previous studies among HCV+ populations and PWIDs.[28,46] Overall, treatment adherence was 71.3%, slightly lower than has been reported in literature.[10,32] However, these data remain impressive considering this is a highly active injecting population with significant rates of homelessness, incarceration and mental health problems. Weekly nurse-led follow-up visits and use of contingency management may have influenced adherence. The results add to growing evidence that HCV treatment can be successfully provided through community-based models.[9,10,23,24,44,47]

Our results demonstrate some association between OST and higher rates of adherence. This is consistent with findings from a previous meta-analysis,[32] with implications for the role of addiction treatment alongside HCV care. Shorter treatment duration was associated with improved adherence (12/16- vs 24-weeks) ($P$ = 0.047). This has important implications for adherence on current DAA treatment regimens which are now only 8- or 12-weeks. Re-infection rate decreased with age ($P$ = 0.063), consistent with existing literature.[36,39] There was little association between other hypothesized factors and adherence or re-infection.

## 5 | CONCLUSION

PWID were successfully recruited, treated and followed up from a community NSP. However, we also report higher rates of re-infection than many other studies. This demonstrates that we have successfully engaged with and treated a high-risk injecting population who should be targeted as part of any successful treatment as prevention (TasP) strategy. Scaling-up the intensity of harm reduction and HCV treatment provision is needed to minimize re-infection and reduce HCV transmission in the population.

## ACKNOWLEDGEMENTS

The study was funded jointly by the Scottish Government department of Public Health and Janssen Pharmaceuticals. Roche donated interferon alpha and ribavirin. We thank Tayside Clinical Trials Unit for their help with collection and management of the study data.

## CONFLICT OF INTEREST

BS acknowledges honoraria for lectures from Abbvie, MSD and Gilead. SH acknowledges honoraria for presentation from Gilead. PV acknowledges honoraria for meetings and conferences from Gilead, MSD, Abbvie. MH acknowledges honoraria for meetings and conferences from Gilead, MSD, Abbvie. JFD has grant/research support from Abbvie, Bristol-Myers Squibb, Boehringer Ingelheim, Gilead Sciences, GlaxoSmithKline, Janssen, Merck Sharp & Dohme, Roche and received speakers honoraria from Abbvie, Bristol-Myers Squibb, Boehringer Ingelheim, Gilead Sciences, GlaxoSmithKline, Janssen, Merck Sharp & Dohme, Roche.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**How to cite this article:** Schulkind J, Stephens B, Ahmad F, et al. High response and re-infection rates among people who inject drugs treated for hepatitis C in a community needle and syringe programme. *J Viral Hepat*. 2018;00:1–10. https://doi.org/10.1111/jvh.13035