High rate of hepatitis C re-infection following antiviral treatment in the North East England Prisons

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Abstract

Introduction: To achieve elimination of hepatitis C (HCV), a critical group to prioritise for diagnosis and treatment is the prison population, where HCV prevalence is high. A universal offer of blood borne virus testing (UOBBVT) program and a new treatment pathway was introduced to seven North East England (NEE) Prisons. Our aim was to assess: 1. the proportion of individuals with active HCV commencing direct acting antivirals (DAAs); 2. the outcomes following DAA treatment; 3. the re-infection rate following sustained virological response (SVR).

Methods: Data was collected prospectively on BBVT uptake, HCV positivity, HCV treatment outcomes and reinfection from March 2016 onwards.

Results: 8,538 individuals had BBV testing. 612 (7.2%) and 374 (4.4%) were HCV antibody positive HCV RNA positive, respectively. Ultimately, 266 (71%) individuals commenced DAAs. 111 achieved a documented SVR (42%), 17 (6%) failed treatment, 30 (11%) were still on treatment or had not reached 12 weeks post-treatment at time of analysis, and 108 (41%) were lost to follow up. In those with a known outcome (n=128) 87% achieved SVR. Worryingly, of those who achieved SVR, 21 (19%) were subsequently identified as having been re-infected (median time from SVR to documented reinfection 13 (range 7-25) months). The reinfection rate was 0.406 cases per person-year follow-up.

Conclusions: Implementation of a UOBBVT program and new treatment pathway resulted in increased diagnosis and treatment of HCV in the NEE prison population. However, the high HCV re-infection rate suggests a need to improve harm reduction approaches.

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Introduction

Chronic Hepatitis C virus (HCV) infections are estimated to have directly contributed to 1.34 million deaths worldwide by 2015, a greater number than for many other highly prevalent global infections, such as HIV and Tuberculosis (1). Currently, in England there are an estimated 113,000 individuals infected with HCV, with injecting drug use being a major risk factor for acquisition (2). A key objective of NHS England is to upscale testing for, and treatment of, HCV, aiming to eliminate HCV from England by 2025. This has become a realistic target given the wide availability of direct acting antiviral drugs (DAA), with which, more than 95% of HCV-infected individuals treated with an 8- or 12-week course of a once a day oral combination of DAAs achieve a sustained virological response (SVR), defined as a HCV RNA negative test 12 weeks post-treatment (3). A particular focus of elimination efforts has been to address the burden of infection in the prison population, which has an estimated HCV prevalence of 3-7%, much higher than the general UK population (0.5%) (4). The high prevalence of HCV in prisons is explained principally by the fact that an estimated 60% of injecting drug users have been incarcerated at some point during their lives, and 68% of individuals in prison have injected drugs within the last year (5).

In March 2016, a formally commissioned universal offer of blood borne virus testing (UOBBVT) program and a new treatment pathway using consultant-led telemedicine clinics and nurse-led in-reach were introduced to Her Majesty's Prison (HMP) Durham and HMP Northumberland. This led to a substantial increase in BBV testing (164 to 1495/year) and a high treatment initiation for those with active HCV (4, 6). Following this successful pilot, the UOBBVT programme and new treatment pathway was rolled out to all seven NEE prisons by April 2017 and a similar BBVT uptake has been seen. The aim of this study was to review the outcomes of individuals diagnosed with HCV within the whole programme, specifically to determine: 1. the proportion of individuals with active HCV who were linked into antiviral treatment; 2. the outcomes following initiation of antiviral therapy for HCV; 3. the re-infection rate following SVR.

Methods

The BBV and testing and treatment pathways

Following a pilot in HMP Durham and HMP Northumberland beginning in March 2016, all seven NEE prisons had fully operational UOBBVT and HCV treatment pathways by April 2017. All BBVT was conducted using dry blood spot testing (DBST) and tested for HCV, HBV and HIV as previously described (4). Individuals in receipt of a positive HCV RNA result on the DBST were reviewed in Prison Healthcare and had a venous sample taken to confirm active infection using HCV RNA along with other pre-treatment blood tests, such as genotype. Any individuals confirmed as being HCV RNA positive were referred to the treatment pathway, which involved an assessment with the viral hepatitis nurse in the prison, followed by consultant review via telemedicine as previously described (4). Following discussion in the multidisciplinary team meeting (MDT) patients were offered DAA treatment in line with NHS England recommendations. Treatment was initiated and monitored within the prison by viral hepatitis nurses and prison staff. In order to determine the outcome of treatment, a blood test was taken 12 weeks post-DAA treatment. Individuals who had negative HCV RNA 12 weeks post treatment were considered to have achieved SVR. Blood was taken opportunistically to test for re-infection in those achieving SVR either in prison or the community. Re-infection was defined as a positive HCV RNA blood test following a documented sustained virological response (SVR12) using standard venous blood testing. The reinfection rate was reported as the number of cases of reinfection per person years follow up.

Data was collected prospectively from the start of the program in March 2016 until the end of February 2019 and includes: HCV antibody and HCV RNA positivity; numbers of HCV RNA positive individuals referred to the HCV service, seen by the service, discussed in the MDT meeting and subsequently treated; and their outcome from treatment. For individuals who started antiviral treatment, basic demographic data was collected including gender, age, stage of liver fibrosis and HCV genotype. The regional Virology Laboratory database, which includes results for all patients treated within the prison and for all patients within our region, was accessed for all treated patients to assess and ascertain SVR and re-infection data up to

the end of February 2019. If individuals were released from prison to a residence out of our region then we were not able to access their virology information. This service review was approved by the Newcastle-upon-Tyne Hospitals NHS Foundation Trust clinical governance department (project 8083).

Results

Since the start of the program, 8,538 inmates had BBV testing and their outcomes are shown in Figure 1. Of those screened, 612 (7.2%) were HCV antibody positive and 374 (61.7% of HCV antibody positive and 4.4% of total) were identified as HCV RNA positive, indicating active infection. Of the HCV RNA positive individuals, 356 (95%) were referred to the service and 332 (89%) were discussed at MDT meeting, and ultimately 266 (83% of those discussed at MDT and 71% of those testing HCV RNA positive) were commenced on antiviral treatment. Early release from prison prior to treatment initiation was the main reason for individuals not commencing antiviral treatment.

Of the 266 individuals who started treatment (86% male; 81% aged 30-50 years; 96% non-cirrhotic; 57% genotype 3 and 38% genotype 1), 111 achieved a documented SVR (42%), 17 (6%) failed treatment (6 relapsed, 11 did not complete treatment), 30 (11%) were still on treatment or had not reached 12 weeks post-treatment at the time of analysis, and 108 (41%) are unknown due to loss to follow up. In the treated patients with a known outcome (n=128), 87% achieved SVR. Of those 108 with an unknown outcome, 17 (16%) were released on treatment, 15 (14%) transferred to another prison outside the NEE on treatment and the others (n=76, 70%) completed treatment within the prison but were released before 12 weeks post-treatment, resulting in the outcome of treatment not being documented in the prison.

Worryingly, of those who achieved SVR, 21 (19% of all SVRs and 44% of those who had follow up HCV RNA testing after SVR [n=48]) were subsequently identified as having been re-infected. The median time from SVR to documented reinfection was 13 months (range of 7

months to 25 months). The rate of reinfection was 0.406 cases per person-year follow-up (total 52 person-years follow up).

Discussion

In this review we have demonstrated a high percentage of initiation of HCV treatment (71%) following diagnosis of active HCV within the NEE prisons using a treatment pathway that incorporates nurse led in-reach and consultant delivered telemedicine clinics. This represents a large increase when compared with previous treatment data in our prisons (14%) and data reported elsewhere (4,6). However, approximately 30% of HCV viraemic individuals still don't commence antiviral treatment, mainly due to short sentences. Hopefully, the planned introduction of more rapid point of care diagnostics in our prisons, followed by immediate initiation of pangenotypic drugs in those with HCV viraemia will improve treatment rates further. The percentage of patients with a known outcome achieving SVR was acceptable at 87%, but unfortunately in 41% (n=108) of those who started antiviral treatment we were unable to document their response to treatment due to their release from prison prior to the end of the follow up period. The majority of these patients completed their treatment while in prison so are likely to have achieved SVR. Other studies in the prison setting have also had high loss to follow up (7). In order for us to ultimately prove elimination of HCV we will need to develop better approaches to documenting treatment outcomes in those released from prison.

Another important finding from this review was the high rate of re-infection seen in patients who achieved SVR. Overall, of those individuals with a documented SVR, 19% had a re-infection and the median time to documentation of re-infection was 13 months. Given that these individuals were opportunistically retested post-SVR rather than being systematically screened, the actual *proportion* becoming reinfected could be even higher, particularly since 44% of those who actually had follow up HCV RNA testing post-SVR had reinfection. The reinfection *rate* could be an overestimation though because individuals with ongoing risk of re-exposure to HCV may be more likely to get HCV RNA testing. Unfortunately, we were also

unable to specifically determine where the reinfection occurred in these individuals. This rate was higher than reported in previous studies, however reflects projected reinfection incidence also reported in these studies (8). Given that some injecting drug users may return to heightened levels of injecting activity following release from prison, a high rate of reinfection may not be surprising, and this highlights that released prisoners who go on injecting likely contribute significantly to the burden of new infections. Although all patients with HCV in the prison are given harm reduction advice to reduce their risk of re-infection, this review underlines the need for us to improve these measures. Integrating improved drug and alcohol services to our treatment pathway, including adequate sterile needle and syringe programs, improved access to opiate substitution therapy and addiction counselling, may prove important in reducing transmission within the prisons. The high rate of reinfection does highlight that we are treating individuals who may present a higher risk of HCV transmission to others. Therefore, it remains vital that they are offered re-treatment where necessary. Moreover, we should develop a systematic approach to those with reinfection and perform contact tracing to identify other HCV infected individuals in their injecting group and treat them with antivirals at the same time to reduce the risk ongoing transmission.

In conclusion, a universal offer of BBV testing using DBST alongside a well-defined referral and treatment pathway has led to many new diagnoses, with a high proportion of these individuals receiving antiviral treatment with acceptable SVR rates. There remains room for development in the uptake of testing, alongside a more rapid and comprehensive treatment pathway, to reduce HCV transmission in the prison setting. Furthermore, HCV re-infection rates are high so we must actively retreat these individuals and expand our harm reduction approaches.

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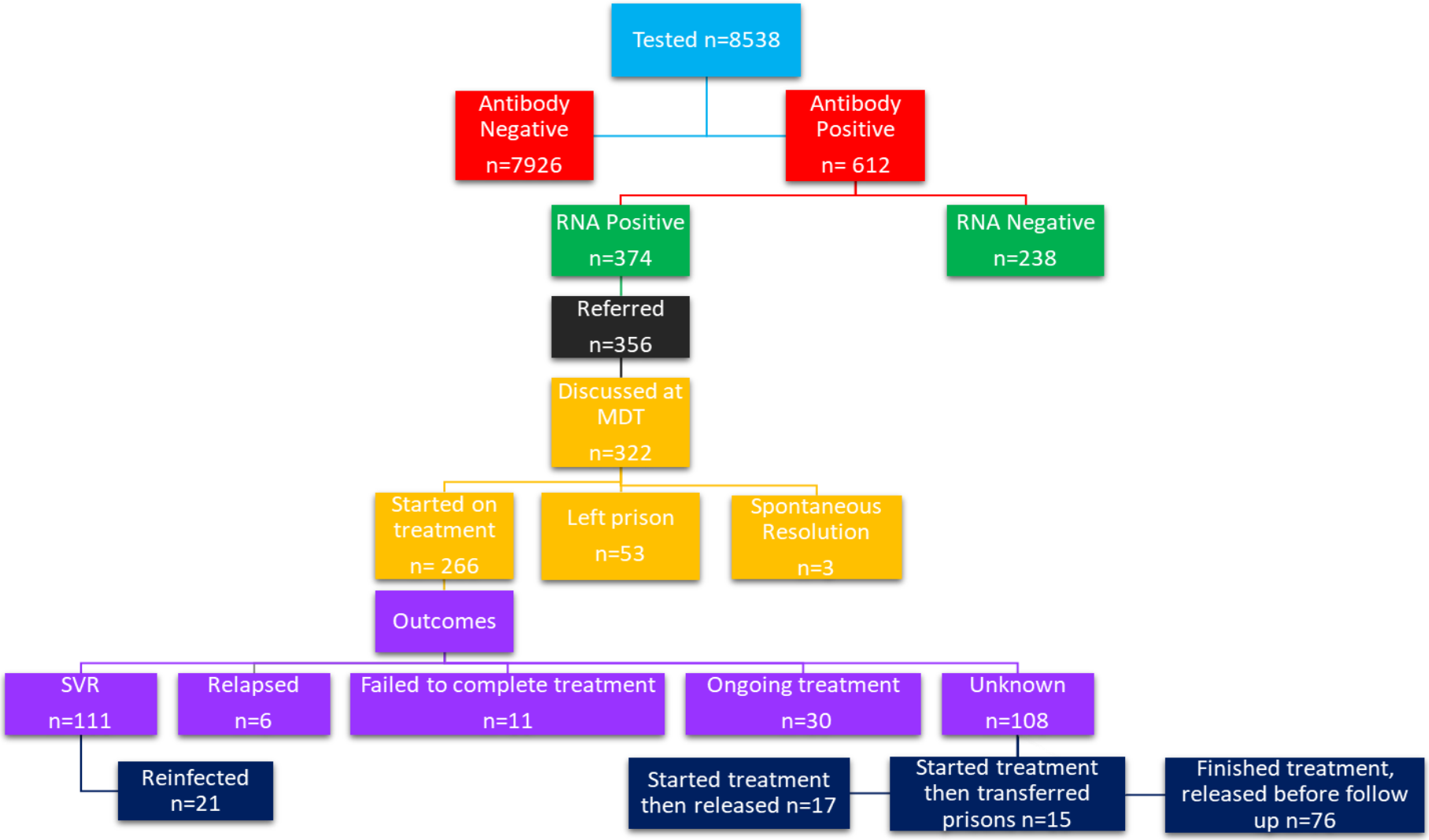
Figure legends

Figure 1. Overall outcomes of the pathway from testing to treatment.

Flowchart illustrating the number of individuals at each stage of the pathway from testing through to treatment, including outcomes of treatment. This includes all patients, both pre-existing and new receptions, who received treatment since the initiation of the program between March 2016 to the end of February 2019. SVR= Sustained virological response. An unknown outcome refers to individuals started on treatment without the necessary follow up testing at 12 weeks post treatment to assess treatment response.


Tested n=8538
Antibody Negative n=7926
Antibody Positive n= 612
RNA Positive n=374
RNA Negative n=238
Referred n=356
Discussed at MDT n=322
Started on treatment n= 266
Left prison n=53
Spontaneous Resolution n=3
Outcomes
SVR n=111
Relapsed n=6
Failed to complete treatment n=11
Ongoing treatment n=30
Unknown n=108
Reinfected n=21
Started treatment then released n=17
Started treatment then transferred prisons n=15
Finished treatment, released before follow up n=76