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i. Title: Detection, stratification, and treatment of hepatitis C positive prisoners in the United Kingdom prison estate: Development of a pathway of care to facilitate the elimination of hepatitis C in a London prison.

ii. Running title (40-character limit): Linkage into care of HCV positive prisoners.

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vi. Abstract:

The United Kingdom is committed to eliminating hepatitis C virus (HCV) infection by 2025. The prison estate provides an opportunity to identify and treat HCV-positive individuals in a high-prevalence environment. We designed and implemented a pathway of care within a London prison to diagnose, stratify, and link HCV-positive prisoners into care. This study was a two-phase case study of a HCV care pathway. New arrivals to the prison were offered blood-borne virus screening with dried blood spot testing at their secondary health check. Those with active infection completed disease stratification tests and were reviewed at a weekly hospital-based multidisciplinary team meeting to determine management. In Phase 2 the pathway was re-designed to improve testing and the referral of HCV-positive prisoners into treatment. Over the 30 month evaluation 12,946 people were received in the prison. During Phase-1, 19.6% of new arrivals completed blood-borne virus testing, with 7.3% identified as HCV-positive. Just 8.3% of HCV-positive individuals were treated or referred for treatment in Phase-1. During Phase-2, 30% of new receptions completed BBV testing and 3.9% were identified as HCV-positive. Linkage into care was improved, with 38.9% treated or referred during the second phase. Poor access to testing and referral to treatment limit the effectiveness of care provision for prisoners with HCV. Elimination of HCV in prisons requires local service configuration to ensure high uptake of testing, with all HCV-positive cases then offered treatment during custody or referral on to treatment after release.

Key words:

1. Hepatitis C
2. Prisoners
3. Diagnostic screening programs
4. Diagnosis
5. Liver Cirrhosis

vii. Main Text:

National Health Service England (NHSE) has targeted the elimination of hepatitis C virus (HCV) as a public health threat by 2025¹, 5 years earlier than the goal set by the World Health Organisation (WHO)². Given that 24-76% of those with HCV are unaware of their illness^{3,4}, opportunistic screening of asymptomatic individuals to detect and treat HCV is crucial to achieve this goal.

Almost 200,000 people pass through the United Kingdom (UK) prison estate annually^{5,6}, where HCV seroprevalence is estimated to be between 7-25%⁷⁻¹⁰, compared to <1% in the community⁸⁻¹⁰. This disparity can be explained by the fact that a large proportion of the prison population in the UK are males in midlife, a group that has higher rates of HCV infection than other demographic groups¹¹. Secondly, injecting drug use (IDU) is common amongst incarcerated persons, with one study reporting that 64% of prisoners injected drugs until reception at a prison¹². Considering 80-90% of HCV transmissions in the UK are thought to occur through IDU^{8,13,14}, prisons therefore offer a unique public health opportunity to engage at-risk persons, who are typically underserved by healthcare services in the community¹⁵.

In England, health authorities decided to capitalise on this public health potential by implementing routine opt-out blood-borne virus (BBV) testing for all newly incarcerated prisoners¹⁶. This strategy was ratified within the National Partnership Agreement between Public Health England (PHE), NHSE, and Her Majesty's Prison and Probation Service (HMPPS) in 2013, with phased implementation beginning across the estate in 2014. The programme included targets designed to increase testing of new receptions to a prison from 4% to at least 50%¹⁷ and therefore a significant increase in newly diagnosed HCV cases was anticipated from the English estate.

Managing these cases fell to 22 Operational Delivery Network (ODNs): regional structures led by a local hospital and introduced in 2014 as a means of controlling access to direct acting antiviral (DAA) treatments. DAAs, which are short course (8-12 weeks), all-oral treatments that have minimal side effects and excellent cure rates (80-90%)¹⁸⁻²⁰, have dramatically increased the feasibility of treating HCV infection, particularly within the prison estate.

However, prison healthcare services and their local ODNs needed to implement pathways of care that effectively link those diagnosed via opt-out testing with DAA-based treatments. In London we piloted a pathway of care within a single prison, to trial an approach and inform the roll-out of opt-out BBV testing and associated treatment pathways across the rest of the London estate. This pathway had three objectives:

1. To test at least 50% of new arrivals at the prison;
2. To rapidly stratify seropositive individuals and determine their treatment plan with the ODN;
3. To deliver treatment to those prisoners who could complete the appropriate drug regime during their period of incarceration, to refer those moved or released to an area under the jurisdiction of a different ODN, and to re-engage those released into the local community for treatment.

Methods:

Study design:

We undertook a case-study of a trial pathway of care to improve the diagnosis and treatment of HCV within a prison setting. This study drew on Action Research²¹ as a methodology, with iterative implementation, evaluation, and pathway modification stages. Local commissioners and prison healthcare stakeholders provided direct input into the pathway assessment and redesign process²². Here we report on the first two phases of the pathway.

Setting:

This study was completed in a 1,250 capacity all-male “category B” local London prison, which served nearby courts and held short-stay sentenced and unsentenced prisoners. A local prison was chosen because people who inject drugs (PWID), at high risk of HCV, tend to receive shorter sentences (averaging four months in the UK)²³, and the rapid-population turnover necessitates a pathway that can progress patients from diagnosis to cure quickly. At the time of evaluation almost 60% of prisoners spent 3 months or less in the prison (79% <6 months) before being released, bailed, or transferred to other prisons for longer sentences.

Phase-1 pathway:

The original pathway (Phase-1) ran from December 2015 to February 2017. Prisoners were offered dried blood spot testing (DBST) at secondary screening, a clinic aimed at establishing a baseline health evaluation and typically occurring within 72 hours of entrance. If the individual accepted, the procedure was completed during the consultation (figure 1).

Samples were sent to a laboratory and tested for HCV antibody (anti-HCV). A reflex polymerase chain reaction (PCR) test for HCV RNA was performed on reactive samples and HCV RNA-positive individuals were invited for a venous blood draw to complete stratification tests to inform treatment allocation. Tests included: genotype, viral load, full blood count, urea & electrolytes, liver function tests, clotting factors, and fibrosis assessment using the Enhanced Liver Fibrosis test (ELF)²⁴.

All HCV RNA-positive cases were referred to a Clinical Nurse Specialist (CNS) from the local ODN, who visited the prison weekly. Those deemed eligible for treatment by the CNS were then reviewed at a weekly ODN multidisciplinary team meeting (MDT), comprising viral hepatology consultants, pharmacists, and nurses.

Patients were allocated to commence treatment, provided that their sentence was long enough to permit completion of the medication regimen, and drugs were provided to prisoners by the ODN CNS. If due for transfer to another prison, they were referred to the appropriate ODN and prison medical team. If due for release to a different region within 3 months, they were referred to the appropriate ODN and their GP (if registered). If released into the surrounding community, it was the CNS's responsibility to initiate re-engagement and treatment.

Phase-2 pathway:

Pathway redevelopment took place in March 2017, informed by an analysis of Phase-1 outcome data and a realist process evaluation, which involved semi-structured observation of pathway procedures, interviewing stakeholders (staff, commissioners, and service users), and reviewing models of best practice reported in the literature²⁵. The

Pathway re-design to address barriers to effective care

Three core challenges were identified through the evaluation of the initial pathway. Regarding testing, new arrivals were frequently being missed or refused to attend secondary screening. In addition, confusion around how to deliver an opt-out test offer was noted amongst healthcare staff. To address this problem, prison healthcare staff that regularly ran secondary screening were offered two additional training sessions on delivering opt-out testing (figure 1). A script outlining a model opt-out BBV test offer was also developed and disseminated across the prison²⁵.

To address the difficulties encountered with prisoner non-attendance, a new engagement strategy was developed. The prison healthcare team, comprising a manager, a nurse and the ODN CNS and doctor developed a waiting list so that new arrivals could be tracked and any who missed testing could be engaged. In addition two healthcare assistants (HCAs) were provided with DBST equipment and encouraged to offer testing when prisoners were out of their cells (e.g. when attending the gym, during social time, or visiting the prison library). Prisoners accepting testing were taken to a confidential environment (usually an office or clinic room), where testing was performed. All tests completed in this manner were cross-referenced against the waiting list. Due to security considerations, out-reach testing was not completed on the substance misuse wing.

The source of the delays between diagnosis and ODN MDT assessment were attributed to delays in the receipt of laboratory results and difficulties encountered by the CNS in accessing the prison (due to heightened security) and, once inside, the prisoners (who frequently did not arrive at pre-arranged clinics) (figure 1). To streamline the assessment process, the prison sexual health nurse took ownership of managing patients and referring HCV-positive cases directly to the ODN MDT. The CNS took on a supervisory role, providing peer support to the sexual health nurse.

Finally, attempts were made to engage the National Probation Service and regional Community Rehabilitation Companies (probation contractors responsible for low-risk offenders) to acquire their support in following-up patients in the community, taking advantage of the requirement for prisoners who are detained in custody for more than 2 days to serve a minimum of 12 months under community supervision. However, information governance concerns prevented this partnership from developing.

Data collection:

Baseline data collection took place from December 2015 to February 2017. Pathway re-development took place between March and September 2017 and second phase data were collected from March 2017 to May 2018.

Templates for recording data on SystmOne (the clinical IT system in use throughout the English prison estate) were developed by the NHS North East Central London Commissioning Support Unit. These templates captured data for the testing, stratification, and referral stages of the pilot pathway. The treatment stage of the pathway was covered by the Royal Free London NHS Foundation Trust's Microsoft Access database "Priority-C", designed by DM.

SystmOne reports, created by the prison's data analyst, were used to extract data on the testing, stratification, and referral stages of the pathway. This information was sent periodically by secure transfer within the NHS network to the hospital-based team, who manually cleaned the data and hosted it in a central excel database. Treatment data were extracted from Priority-C by the hospital-based research team.

Ethical approval:

Ethical approval was not required for this study as it was judged to be part of a service evaluation using the UK Medical Research Council's tool "Is my project research" and was registered as such.

Results:

A total of 12,964 receptions were processed during the 30-month evaluation period. Figure 2 outlines prisoner numbers at different audit points.

Phase-1:

During Phase-1 6,450/6,767 (95.3%) of receptions remained in the prison long enough to attend secondary screening. However, only 2,795 offers were made (43.3% of those eligible), whilst 1,324/2,795 prisoners (47.4%) accepted and completed a DBST. Of the prisoners tested, 96/1,324 (7.3%) were identified as HCV-positive, of which 79/96 (82.3%) completed stratification tests. Thus 0.015% of receptions were identified as HCV positive. Despite planning to offer testing to

all people entering the prison, those entering the Substance Misuse wing were less likely to be offered testing due to a failure to engage the healthcare team on this wing.

Referrals to the hospital CNS were received for just 22/96 (22.9%) of the HCV RNA-positive prisoners. Where a referral was received, 11/22 (50%) were reviewed in prison by the CNS and 10/11 (90.9%) of these HCV RNA-positive cases were referred to the ODN MDT, representing just 10.4% of all HCV RNA-positive cases detected in prison. Following MDT review, 3/10 (30.3%) were treated, 5/10 (50%) were referred, and 2/10 (20%) had contraindications to treatment.

In Phase-1, just 10/96 (10.4%) of the HCV-positive prisoners were managed in accordance with the pathway as planned, while 86 cases (89.6%) had no access to treatment following diagnosis. Only 17/86 (19.7%) HCV-positive prisoners failed to complete the disease stratification tests necessary for treatment allocation. The greatest loss of HCV RNA-positive individuals occurred at the point of referral from prison healthcare to the CNS (66.3% attrition). A further 11/96 (12.8%) of HCV RNA-positive prisoners, representing 50% of total CNS referrals, were lost between CNS referral and CNS visit.

Evaluation of Phase 1 of the pathway identified barriers that are summarised and attributed to specific stakeholders in Table 1. Potential solutions derived from work with stakeholders informed by reviews of the relevant literature are presented as potential solutions in Table 1. Where possible these solutions were implemented in Phase 2.

Phase-2:

Following pathway reconfiguration, more test offers were made (58.4%) and a greater proportion of new arrivals completed BBV testing (29.9%) (figure 2). Of those tested, 72/1,854 (3.9%) were found to be HCV RNA-positive, a significant drop compared with Phase-1. Out of those identified with active infection, 46/72 (63.9%) completed stratification tests (18% fewer than in Phase-1) and 45.8% of HCV RNA-positive prisoners were referred to ODN MDT.

Thirteen prisoners were not referred to the MDT due to clerical issues relating to a lack of administrative capacity within the prison and a lack of robust electronic systems. Thus 35.4% more prisoners were referred for treatment in Phase-2 compared to Phase-1. At the time of audit,

13/72 (18.1%) of all HCV RNA-positive prisoners referred in Phase-2 had commenced treatment, (representing a 4-fold increase compared to the original pathway), all of whom subsequently achieved a sustained viral response (SVR).

Of the remaining prisoners discussed at the ODN MDT, 15/72 (20.8%) had been referred to another ODN and 5/72 (6.9%) were awaiting treatment commencement. Subsequently 4 have achieved SVR and 1 has repeatedly defaulted from treatment due to mental health problems. In Phase-2, the allocation of prisoners referred to the ODN for treatment 13/33 (39.4%), or referral to another ODN 15/33 (45.4%) mirrored Phase-1.

Despite the lower HCV sample positivity in the Phase-2 cohort (3.9% v 7.3%), a significantly higher proportion of HCV-positive patients had been treated or referred at the time of audit (28/72 v 10/96; $X^2=19.056$; $p=0.00001$ Fisher exact). This number increased after the census date to include 4/5 prisoners who were awaiting treatment and at least 3/15 prisoners referred elsewhere.

Discussion:

Prisons offer a unique public health opportunity to identify HCV-positive individuals in an at-risk group, who typically engage poorly with healthcare services. Since the licensing of DAAs, HCV treatment can be delivered safely and effectively in prisons^{18-20,26,27}. Failure to identify and treat HCV-positive prisoners increases the risk of transmission to other inmates²⁸ and dissemination in the community following release^{26,29}.

This pathway was designed to increase the identification and treatment, or referral of HCV positive prisoners in a local London prison. Evaluation of the Phase-1 pathway identified opportunities to improve diagnosis and treatment rates, with implemented changes delivering better cure rates. Retraining healthcare staff in how to test, providing a script for the opt-out offer, encouraging testing after secondary screening, and empowering the prison healthcare staff to refer directly to the ODN MDT led to both an improvement in the number of new arrivals tested for BBV infection (Phase-1 = 19.6%; Phase-2 = 29.9%), and the number of HCV patients handled appropriately by the pathway (Phase-1 = 10.4%, Phase-2 = 45.8%).

However, modifications to the pathway did not improve all outcomes. Reasons for a drop in the proportion of those identified with active infection completing stratification testing during Phase-2 were unclear. Staffing shortages, changes amongst the custodial team, frequent “lock downs” (locking all prisoners in their cells), and a breakdown in handing out “healthcare slips” (appointment notifications for prisoners) were all reported by the prison healthcare team as potential justifications.

The difference in HCV RNA prevalence between Phase-1 (7.2%) and Phase-2 (3.9%) was also significant. Phase-2 test positivity was comparable to the HCV seroprevalence reported during an audit of opt-out testing in a North-eastern English prison³⁰, but was lower than a recent study looking at BBV testing across West Midland prisons (anti-HCV = 9.3%)³¹ and national sentinel surveillance testing from 2013 (9.4%) to 2017 (8.0%)³²⁻³⁵. This decline could have occurred if targeted testing rather than screening was taking place during Phase-1, if the prison experienced a change in incarceration patterns, or if pathway reconfiguration, as well as other contextual changes, resulted in the underrepresentation of high-risk prisoners during Phase-2. It was noteworthy that security considerations on the substance misuse wing limited testing activities during the both phases. This may have resulted in prisoners at a higher risk of infection being missed, while lower-risk prisoners, completing out-reach screening on other wings, may have ‘diluted’ the HCV seroprevalence.

Nevertheless, testing remained below NHSE targets (50-75%)¹⁷, whilst a high proportion of HCV patients were still not being managed appropriately due to restricted access to prisoners, prisoners refusing to attend clinics, and problems re-engaging patients released from the prison. These barriers stemmed from a failure to engage all stakeholders necessary for successful delivery of the pathway (figure 2), such as prison officers and the substance misuse team that effected both phases of the pathway. For example, a lack of dedicated officers to assist the healthcare team left them reliant on the good will of busy officers, who were focussed on ensuring safety and security within the prison. Allocating prison officers to support healthcare staff in engaging, testing, and treating prisoners would therefore likely improve treatment rates within the prison.

The refusal of prisoners to attend clinics also introduced delays²⁵. Simple changes, such as ensuring clinics do not clash with other preferred prison activities like “association” (socialising)

or gym access, can help to encourage attendance²⁵. Strategies such as making attendance at secondary screening mandatory in order to be medically cleared for work or gym attendance, or providing prisoners with incentives to attend, should also be explored.

Finally, methods to shorten the pathway need to be considered. The requirement for patient assessment and referral to be completed by the ODN CNS resulted in a loss of 87.3% of stratified HCV-positive patients during Phase-1. By training the prison's sexual health nurse to complete stratification tests and then refer prisoners directly to ODN MDT reduced attrition to 28.3%.

Biomedical innovation may also help to shorten the pathway. Use of point-of-care HCV antibody and PCR testing would obviate time waiting for diagnostic tests to be processed by a laboratory³⁶. Use of pangenotypic DAAs, which are cost-effective and widely reimbursed in other developed nations, could also reduce the test burden and shorten the journey to treatment.^{26,37,38 39}. Training prison medical staff to initiate and monitor HCV treatment under the supervision of broader national public health programs should be considered^{39,40}. This would require provision of adequate resources and support from NHS ODNs⁴¹.

In summary, the changes made between Phase-1 and Phase-2 were largely positive but limited in scope. Although changes to care delivery and the inclusion of biomedical innovation can help shorten the pathway, greater efforts are required to include custodial and probation services in the elimination effort. If prisons are to meet their public health potential in terms of diagnosing and treating HCV infection, partnership between custodial services, healthcare services, and patients is required.

Limitations:

The absence of a centralised electronic patient record system, linking prison and community healthcare, means data for this service evaluation were collected from a range of sources and required manual cleaning, which may have introduced errors to overall counts. Unreliable prison data has previously been noted in relation to HCV testing and treatment⁴¹.

Conclusions:

Screening 30% of receptions and treating 18% of HCV RNA-positive prisoners will not adequately support the goal of HCV elimination in the UK by 2025^{1,2,29,42}. Small-scale pathway reconfiguration can improve performance. However, if the public health potential of English prisons for HCV elimination is to be fully realised, systemic change, where custodial and probation services become active collaborators of testing and treatment initiatives, is required. Patients may also require incentives in order to prioritise engaging with healthcare services at the level required for elimination.

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ix. Table:

Table 1. Barriers to hepatitis C care pathway delivery within a local English prison, related to specific stakeholders, and potential solutions.

Stage	Stakeholders	Barriers	Solutions
Testing	Officers	Prison officers will naturally prioritise prison tasks for which they are held directly responsible. This can result in delayed clinics, not all prisoners being brought to clinic, or some clinics being cancelled	1) Provide dedicated prison officers to support testing clinics
	Prisoners	Not all prisoners prioritise attending testing clinics	1) Ensure clinics do not clash with other desirable activities 2) Provide incentives to encourage attendance
	Prison healthcare staff	Some healthcare staff may not know how to deliver opt-out testing or are not motivated to do so	1) Ensure regular training is provided for staff 2) Provision of an opt-out offer script 3) Encourage good testing practice via reward schemes
Pathway progression	Officers	Prison officers will naturally prioritise prison tasks, creating delays to engagement	1) Provide dedicated prison officers to support assessment clinics
	HCV patients	Not all patients will prioritise or want to engage with care	1) Build positive relationships with patients where treatment can be encouraged 2) Use of incentives to encourage engagement with the pathway
	Healthcare	Reliance on in-reach support from a local operational delivery network can create delays if access to patients or the prison is restricted. Waiting for diagnostic and assessment tests to be processed by a laboratory introduces unavoidable delays	1) Train prison healthcare staff to operate as much of the pathway within the prison as possible 2) Use of point-of-care testing to reduce the time between testing and diagnosis 3) Use of pangenotypic direct acting antiviral obviates need for genotype for treatment decision. Use of the Enhanced Liver Fibrosis (or other serological assessment of fibrosis) may be beneficial when access to transient elastography limited
Re-engagement	HCV patient	Upon release, many individuals will prioritise re-integrating with society or may not be in the mental or physical position to prioritise treating their infection	1) Healthcare services need to work with housing and social services to help ensure a stable transition into the community 2) Use of incentives may help to encourage patients to re-engage with care 3) Building trusting relationships with patients may help encourage them to re-engage with treatment 4) Patients require a simple means of self-referring into their local operational delivery network
	Probation	Probation services could provide logistical support for re-engaging newly released patients, but they are not incentivised to work with operational delivery networks and information sharing issues may frustrate partnership working	1) Supporting the delivery of healthcare needs to be included in the contracts of privatised probation services. Clear national guidance should be developed on how probation services are expected to support patient re-engagement
	Courts	Patients that have not received a sentence (i.e. on remand) may be released from court without warning. If these individuals have received no sentence, they will not be required to engage with probation services	1) Healthcare services operating within courts need to work with local operational delivery network and prison healthcare partners to ensure that HCV patients released directly from the court are provided with the same information and support for re-engagement than those individuals released directly from a prison

x. Figure legends:

Figure 1: Format of a hepatitis C care pathway, implemented within a local London prison, during two phases of operation (ODN = operational delivery network; CNS = clinical nurse specialist, MDT = multi-disciplinary team meeting). Times provided for the Phase-1 pathway were estimated by prison healthcare staff.

Figure 2: Proportion of prisoners completing each step of the hepatitis C care pathway between two phases of operation. In Phase 1 86 (89.6%) of HCV RNA positive patients were lost from the pathway before treatment or referral for treatment. This number fell to 39 (54.2%) in Phase 2.

xi. Abbreviations:

- BBV – Blood Borne Viral Infection
- CNS – Clinical Nurse Specialist
- DBST – Dried Blood Spot Testing
- DAAs – Direct Acting Antivirals
- ELF – Enhanced Liver Fibrosis test
- HCA – Healthcare Assistant
- HCV – Hepatitis C Virus
- HMPPS – Her Majesty's Prison and Probation Service
- IDU – Injection Drug Use
- MDT – Multidisciplinary Team
- NHS – National Health Service
- NHSE – National Health Service England
- ODNs – Operational Delivery Network
- PHE – Public Health England
- PCR – Polymerase Chain Reaction
- PWID – People Who Inject Drugs
- SVR – Sustained Viral Response
- WHO – World Health Organisation

Phase 1
December 2015 – February 2017

Phase 2
March 2017 – May 2018