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Research Paper

Time matters: Point of care screening and streamlined linkage to care dramatically improves hepatitis C treatment uptake in prisoners in England

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A B S T R A C T

Background: In England, opt-out dry blood spot prison screening for HIV, hepatitis B and hepatitis C (HCV) has been introduced to scale-up access to care. Recent advances in point-of-care HCV diagnostics provide an opportunity to improve diagnosis and treatment uptake. We compared the retention along and time intervals between each aspect of the HCV care continuum for an alternative rapid point-of-care-testing and simplified treatment strategy with existing national opt-out HCV dry blood spot testing and treatment at a large remand prison in West London.

Methods: Between September 2017 and December 2018 universal opt-out dry blood spot HCV testing, clinical assessment and treatment uptake were recorded at Her Majesty's Prison Wormwood Scrubs. Outcomes were compared to a point-of-care-based (salivary Oraquick® anti-HCV screening and Xpert® HCV fingerstick viral load) screening and streamlined treatment pathway offered to all new arrivals to the HMP Wormwood Scrubs substance misuse unit, which ran in parallel to dry blood spot testing between September and December 2018.

Results: During the study period 2442 out of 5239 inmates (46.6%) underwent dry blood spot screening, resulting in 62 (2.6%) HCV RNA positive cases. Thirteen (21.3%) individuals commenced therapy and no viral relapse cases were observed to date. In comparison, 162 out of 181 (89.5%) inmates admitted to the substance misuse unit agreed to rapid point-of-care testing; 20 (12.3%) HCV RNA positive cases. Seventeen (85.0%) of eligible inmates commenced treatment. The median length of stay (90 vs 30 days), time to screening (6 vs 2 days), assessment (14 vs 3 days) and treatment (36 vs 1 day) were shorter for the rapid point-of-care screen-and-treat group.

Conclusion: Current scaling-up of prison dry blood spot HCV screening and treatment in England is sub-optimal. In our setting, the cascade of care is time and resource sensitive and is greatly improved by the introduction of a simplified screen-and-treat strategy.

Introduction

The latest edition of the world prison population list reports that 11 million people are incarcerated globally (Walmsey, 2016). Across England and Wales there are 121 prison estates, responsible for more than 80,000 inmates (Ministry of Justice, 2018). Illicit drug use is an important issue among this population, with a recent systematic review indicating that 58% of people who inject drugs have a history of incarceration (Degenhardt et al., 2017) and particularly high levels of injecting drug use in periods close to being taken into custody and after release into the community (Department of Health; Kamarulzaman et al., 2016). With 90% of hepatitis C virus (HCV) infections considered to be attributed to the people who inject drugs population in England, expanding access to HCV care to people who inject drugs, and consequently people in prison, may play a vital role in achieving the WHO 2030 global hepatitis elimination objectives (Public Health England, 2017a).

However, the understanding of HCV epidemiology among people in prison in the UK is limited by a paucity of existing data, with reports suggesting HCV seroprevalence between 7% and 19% (Taylor et al., 2013; Weild et al., 2000). Until recently attempts to introduce robust HCV screening strategies across the prison estates have been poor, with varying testing practices resulting in overall screening uptake rates of less than 5% (Kirwan, Evans, Sentinel Surveillance of Hepatitis Testing Study, & Brant, 2011; Public Health England, 2017b). In 2013 the need for a blood borne viruses screening policy was acknowledged by Public Health England, NHS England and the National Offender Management Service, with the agreement of a pilot national opt-out dry blood spot blood borne virus screening program. As a consequence, 21% of new arrivals were screened during the implementation phase, leading to the adoption of opt-out dry blood spot testing nationwide from 2016 (Public Health England, 2014). In England, HCV case-finding and treatment programs are overseen through regional 'operational delivery networks', who work closely with prison healthcare teams to deliver a local HCV service.

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In addition to increased screening, linkage-to-care and ultimately access to curative direct acting antiviral therapy remains a key objective. The impact of a successful prison HCV care continuum, in combination with continued opioid substitution therapy, has been shown in mathematical models to have a dramatic impact on both chronic HCV incidence and prevalence in the people who inject drugs community (Stone et al., 2017). Presently, there have been a handful of reports across Europe indicating encouraging HCV cascades of care in prison settings (Vroling et al., 2018) including; telemedicine in the North of England (Morey et al., 2019), en-bloc HCV screening and treatment in Spain (Cuadrado et al., 2018) and a nurse-led model of care across the Australian state of Victoria (Papaluca et al., 2019). However, a recent systematic review of prison HCV interventions underlined a lack of existing linkage-to-care and treatment interventions and emphasized the need for further studies to evaluate models to improve the cascade of care (Kronfli et al., 2018).

Although there is clear merit to dry blood spot use to decentralize sample collection in the community (Coats & Dillon, 2015), technological advances in HCV testing devices have yielded novel point-of-care tools to measure HCV viraemia. In addition to being performed in proximity to the patient and providing a rapid result, point-of-care may be used to change clinical management (Schito et al., 2012). For example, the Xpert® plasma HCV RNA assay, which has recently received World Health Organization prequalification and has been validated to provide a quantifiable result within one hour on whole blood with excellent performance (Grebely et al., 2017; Lamoury et al., 2018; World Health Organisation, 2017). This may aid to further simplify the screening algorithm and improve linkage-to-care in marginalised settings (Fourati, Feld, Chevaliez & Luhmann, 2018).

The aim of this study was to compare, in one of the largest prisons in London (Her Majesty's Prison (HMP) Wormwood Scrubs), retention and time intervals along the cascade of care (from testing to treatment) of two HCV care pathways (universal prison population based opt-out dry blood spot screening and opt-out rapid point-of-care screening using Oraquick® rapid HCV antibody test (Oraquick®) and Xpert® HCV viral load Fingerstick assay coupled with a simplified treatment initiation pathway among individuals admitted to the substance misuse unit to commence opioid substitution therapy.

Methods

Screening setting

HMP Wormwood Scrubs is a large all-male category B prison (medium security), located in West London, with a functioning capacity of 1279 inmates. It is predominantly a remand prison, but also has a dedicated forty-inmate capacity substance misuse unit. Currently, harm reduction in the substance misuse unit is limited to opioid substitution therapy only. A cross-sectional assessment of the HCV care continuum at HMP Wormwood Scrubs for two pathways was conducted (outlined below).

Opt-out blood borne virus screening: conventional NHS England recommended pathway (Public Health England, 2014) (conventional dry blood spot; Fig. 1)

A universal opt-out policy on dry blood spot blood borne virus screening has been in place since early 2017 at HMP Wormwood Scrubs. A primary health screen, which includes offering blood borne virus testing, was performed by clinical staff on arrival in the prison 'first night center'. Dry blood spot testing was subsequently performed by a healthcare assistant (prequalification nurse practitioner) during the more comprehensive 'secondary health screen' on the prison wing, which is expected to be performed within seven days of arrival. These dry blood spot samples were then delivered by mail to the virology laboratory at the Heart of England hospital (Birmingham, UK) for further virological analysis.

Serological and viral tests using dry blood spot

All inmate dry blood spot samples were processed for anti-HIV 1 & 2, anti-HCV antibodies and hepatitis B surface antigen. Reflex confirmatory testing was performed for all seropositive samples; in case of positive HCV antibody both qualitative HCV RNA and genotype measurements were systematically performed. All results were uploaded from the laboratory on the prison electronic patient record (Systm1), which is the universal healthcare operating software used across all prison estates in England. The dates of arrival in prison, dry blood spot sample collection and virology results were obtained from Systm1 and used to calculate time intervals for samples being obtained and for respective virology results to be registered.

HCV clinical assessment

Between September 2017 and December 2018, Imperial College Healthcare NHS Trust (ICHNT) has provided an in-reach Hepatology service on a bi-monthly basis. This involved a clinician-led consultation covering previous risk factor assessment, knowledge of HCV status and previous testing, standard of care phlebotomy (liver and renal function, full blood count, coagulation screen and HCV RNA and genotype (performed in addition to dry blood spot reflex testing)) and assessment of liver disease with transient elastrography (Fibroscan® FS430) by the same trained operator. The time interval between positive dry blood spot HCV RNA result and clinical review was recorded.

Consideration for direct acting antiviral treatment

All inmates eligible for treatment were approved at a bi-monthly regional multi-disciplinary team meeting in accordance with an existing NHS England genotype-specific approved direct acting antiviral therapy. The medication was dispensed by the hospital pharmacy and delivered to the prison in monthly installments. Individuals expected to have a sentence long enough to complete treatment were initiated on therapy, while those with shorter sentences (<3 months) were provided with a laminated contact card at the time of clinical assessment and encouraged to contact the ICHNT team to initiate treatment in the community. The time taken to commence treatment was calculated from date of clinical review to the date of treatment initiation. Where possible, sustained virological response (SVR) samples were obtained at one month (SVR 4) and three months (SVR 12) following completion of treatment.

Rapid alternative 'screen and treat' intervention (alternative point-of-care pathway; Fig. 1)

The successful implementation of the alternative point-of-care pathway was measured by the comparative screening, linkage-to-care and treatment uptake. It focused on expediting time to testing (using point-of-care testing) and treatment (fast-tracked clinical assessment and multi-disciplinary team approval, access to pangenotypic direct acting antivirals and treatment initiation irrespective of length of incarceration). In addition, a specific blood borne virus healthcare assistant was nominated to be responsible for all pre-test counselling and subsequent Oraquick® testing, allowing more accurate recording of testing acceptability. Between September and December 2018, in addition to being offered existing opt-out conventional dry blood spot screening, consecutive individuals admitted on the substance misuse unit for opioid substitution therapy initiation were invited to participate in an opt-out rapid alternative 'screen-and-treat' pathway. Individuals requiring opioid substitution therapy were triaged to the substance misuse unit within twenty-four hours of arrival in prison. As part of the induction assessment, the healthcare assistant performed an

Oraquick® salivary swab in accordance with the manufacturer's guidance, which provided an anti-HCV antibody result within twenty minutes. The ICHNT Hepatology team was informed of any positive result and patients were assessed within one week of referral.

In addition to the clinical procedures described above, a paired ethylenediaminetetraacetic acid (EDTA) venipuncture sample was obtained from each HCV seropositive patient. On the same day as sample collection, 100μl of venous blood was pipetted directly from one of the samples into the Xpert® HCV VL Fingerstick assay research use only (RUO) cartridge (lower limit of quantification >100 IU/mL, lower limit of detection >40 IU/mL; Cepheid, Sunnyvale) by a clinician. This was loaded directly into the GeneXpert® instrument and the time to result was 60 min. The corresponding sample was sent to the local virology laboratory for standard of care plasma HCV viral load and genotyping using the Roche Cobas 6800 system (Risch-Rotkreuz, Switzerland).

All patients with a positive result using Xpert® HCV VL Fingerstick assay were offered interferon-free direct acting antiviral treatment (8–12 weeks), irrespective of length of sentence. Those who agreed were approved via a fast-track multi-disciplinary team. Special dispensation was given to allow flexible prescribing of either the genotype-specific NHS England first-line approved therapy or pangenotypic glecaprevir/pibrentasvir (Gle/Pib).

Therapeutic monitoring continued for the duration of an individual's prison sentence. All medication was dispensed as monthly prescriptions and for those who were released before the end of treatment, an appointment was made at the hospital for the next relevant monitoring interval.

Statistical analysis

Characteristics of the study participants were presented by mean and standard deviation or median and interquartile range (IQR) for parametric and non-parametric continuous variables respectively, while percentage was calculated for the categorical variables. Normally distributed and skewed continuous variables were compared using the independent *t*-test and Mann–Whitney *U* test respectively. Categorical variables were compared using the chi-squared test or Fisher's exact test where appropriate. Prevalence and respective 95% binomial confidence intervals were calculated and statistical significance as a two-sided *P*-value of <0.05. Correlation and agreement between HCV RNA levels using laboratory standard and Xpert® HCV VL Fingerstick was evaluated using Pearson's correlation coefficient and Bland-Altmann analysis, respectively. Microsoft Excel 2010 and SPSS statistical software version 24.0 was used to complete the statistical analyses.

Results

Clinical characteristics of anti-HCV antibody positive patients

The mean age of those testing anti-HCV antibody positive in both dry blood spot and point-of-care screening was similar (43 (standard deviation 10) vs 40 (standard deviation 7) years) and the majority of individuals were born in the UK (42 (75.0%) vs 24 (85.4%). Sixty-two (74.7%) and 20 (83.3%) of individuals undergoing HCV RNA confirmation tested positive, resulting in a chronic HCV prevalence of 2.6% (95% CI 2.0–3.2%) and 12.3% (95% CI 7.7–18.4%) for conventional dry blood spot and alternative point-of-care screening respectively (Table 3). The most frequent genotype reported was 1a (26, 46.4% vs 10, 55.6%) followed by 3a (23, 41.1% vs 7, 38.9%) in both screening settings. Only a minority were HIV co-infected (3 (3.3%) and 3 (10.7%)) in the conventional dry blood spot and alternative point-of-care groups respectively. Of those undergoing clinical evaluation, the median Fibroscan® value was 5.6 kPa (IQR 4.8–7.7) and 5.1 kPa (4.0–8.6), while the liver stiffness measurement suggested cirrhosis in 6 (10.7%) and 3 (13.7%)) of the conventional and alternative point-of-care groups respectively. The most common direct acting antiviral choice of those commencing treatment through conventional screening group was 8 weeks of Sofosbuvir/Ledipasvir (8 W Sof/Led) (5 (38.4%)), while 8 weeks of Gle/Pib was the most popular in the alternative point-of-care screening group (13 (76.4%)). All clinical characteristics for individuals representing both conventional dry blood spot and alternative point-of-care screening groups are presented in Table 1.

Table 1
Clinical characteristics of HCV seropositive patients assessed in both conventional dry blood spot and alternative point of care screening pathways.

Variable	Dry blood spot (*n* = 56)	Point of care (*n* = 28)
Age (mean, standard deviation)	43 (10)	40 (7)
Born in UK *n*, (%)	42 (75.0)	24 (85.4)
Record of diagnosis on system *n*, (%)	28 (30.7)*	23 (82.1)
Aware of Diagnosis *n*, (%)	36 (64.3)	24 (85.7)
Active people who inject drugs *n*, (%)	24 (42.9)	21 (75.0)
Active people who inject drugs, engaged in harm reduction (*n*, %)	12 (50.0)	12 (42.8)
Alcohol excess**, *n*, (%)	15 (26.8)	8 (28.5)
HCV treatment experienced (n, %)	8 (14.3)	1 (3.6)
HIV co-infected (*n*, %)	3 (3.3)	3 (10.7)
Log HCV VL (iU/ml) (median, IQR)	5.7 (4.8–6.6)	5.9 (4.9–6.7)
Genotype distribution (*n*, %)***		
1a	26 (46.4)	10 (55.6)
1b	3 (5.3)	0 (0)
2	2 (3.6)	0 (0)
3a	23 (41.1)	7 (38.9)
4	2 (3.6)	1 (5.6)
Fibroscan® (kPa) (median, IQR)	5.6 (4.8–7.7)	5.1 (4.0–8.6)
Cirrhotic, n (%)	6 (10.7)	3 (13.7)
Treatment****, (*n*,%)		
Elb/Gra 12W	2 (15.3)	1 (5.9)
Gle/Pib 8W	1 (7.7)	13 (76.4)
Gle/Pib 12W	1 (7.7)	0 (0)
Sof/Led 8W	5 (38.4)	3 (17.6)
Sof/Vel 12W	2 (15.3)	0 (0)
Sof/Vel + RBV 12W	1 (7.7)	0 (0)
Omb/Par + RBV 12W	1 (7.7)	0 (0)

* Calculated from total proportion of all anti-HCV antibody cases (including those not clinically assessed, *n* = 91).
** Defined as >18 g of alcohol per day.
*** calculated from all HCV RNA positive patients with available genotype (56/62).
**** Elb/Gra; Elbasvir/Grazoprevir, Gle/Pib; Glecaprevir/Pibrentasvir, Sof/Led; Sofosbuvir/Ledipasvir, Sof/Vel +RBV; Sofosbuvir/Velpatasvir + Ribvirin, Omb/Par + RBV; Ombitasvir/Paritaprevir + RBV.

HCV cascade of care (Fig. 2)

(a) Conventional dry blood spot screening

Between September 2017 and December 2018 there were 5239 prison admissions and 2442/5239 (46.6%) underwent dry blood spot screening as part of the existing 'opt-out' testing initiative. During this period, 91/2442 had a positive result for anti-HCV antibody (3.7%). Of these, 83/91 (91.2%) underwent a viraemia confirmation and 62/83 (74.7%) were chronically infected and 56/62 (90.3%) had a genotype. 56/91 (61.5%) of the anti-HCV positive and 37/62 (59.7%) of the HCV viraemic patients had a clinical assessment, while 1/62 (1.6%) refused to attend clinic and the remainder released before review 24/62 (38.7%). 25/37 (40.3%) were approved to start therapy through the local multi-disciplinary team, with 13/62 (21.0%) actually commencing treatment. SVR 12 data was available for 8 patients, all of whom remained HCV RNA negative (Fig. 3).

(a) *Alternative rapid point-of-care screen and treat pathway*

Between September and December 2018 there were 181 inmates admitted onto the substance misuse wing, 19/181 (10.5%) refused HCV

Table 2
Comparison of length of stay, screening and time to treatment for conventional dry blood spot and alternative point of care pathways.

Time (days)	Dry blood spot*(whole blood anti-HCV antibody, qualitative HCV RNA and genotype)*	Alternative point-of-care*(Oraquick® salivary anti-HCV antibody, Xpert® HCV FS VL and laboratory plasma HCV RNA and genotype)*
Sentence length (median, IQR)	90 (41–182)	30 (13–57)
Arrival to screening test performed (median, IQR)	6 (2–39)	2 (1–3)
Test performed to HCV Ab result (median, IQR)	8 (6–12)	1 (1)
Test performed to HCV RNA result (median, IQR)	15 (12–19)	4 (3–7)*
Test performed to HCV genotype result (median, IQR)	22 (19–26)	17 (13–24)*
Test result** to clinical assessment (median, IQR)	14 (7–41)	3 (0–3)
Clinical assessment to treatment commended (median, IQR)	36 (20–64)	1 (1–2)

* Laboratory HCV RNA and genotype results collected as standard of care but not used to determine treatment initiation.
** HCV RNA for dry blood spot and HCV antibody for alternative point-of-care.

screening and the remaining 162/181 (89.5%) underwent Oraquick® oral salivary testing. 28/162 patients (17.3%) had a positive anti-HCV antibody result, 2 of whom (7.1%) also underwent simultaneous dry blood spot screening. 24/28 (85.7%) had a clinical review (2/28 (7.1%) refused clinical assessment, 2/28 (7.1%) were released), which included HCV viral load testing; 20/24 (83.3%) were confirmed HCV viraemic, with 17/20 (85.0%) subsequently commencing antiviral therapy.

Impact of time on the cascade of care (Table 2)

Inmates enrolled in the conventional dry blood spot group had a longer length of stay in prison (median 90 days (IQR 41–182) compared with inmates in the alternative point-of-care screening group (median 30 days (IQR 13–57)). The median time to dry blood spot being performed was 6 days (2–39 days), while those undergoing alternative point-of-care screening had an Oraquick® salivary test within 2 days of arrival (IQR 1–3). Reflex dry blood spot qualitative HCV RNA confirmation and genotype took a median of 15 days (IQR 12–19) and 22 days (IQR 19–26) respectively from the time a test had been sent to the laboratory. As part of standard of care, plasma HCV RNA and genotype were sent to the local laboratory in the alternative point-of-care group, taking 4 (3–7) and 17 (13–24) days respectively.

In the alternative point-of-care screening group, clinical assessment occurred 3 days (IQR 0–3) after a positive salivary anti-HCV test and HCV RNA confirmation was obtained on the same day using the Xpert® HCV VL Fingerstick assay. In comparison, patients in the conventional screening group were seen 14 days after a positive HCV RNA result (IQR 7–41). Finally, it took a median of 36 days (IQR 20–64) from clinical assessment to commence treatment in the conventional group compared with just one day in the alternative point-of-care group (IQR 1–2).

Discussion

Dry blood spot screening uptake from our study demonstrates a modest improvement in comparison to the original multi-prison dry blood spot implementation pilot in 2016 (47% vs 21%) (Public Health England, 2014). For those with a positive result, retention along the cascade of care is sub-optimal, with a minority of eligible patients (21%) actually commencing treatment. Yet, in line with existing reports (Vroling et al., 2018), treatment outcomes appear to be excellent in the limited number of patients who have completed interval follow up. To our best knowledge our alternative point-of-care 'screen-and-treat' strategy is the first to evaluate point-of-care testing coupled with fast-track access to direct acting antiviral therapy in any prison setting, resulting in higher rates of screening (90% vs 47%), clinical assessment (86% vs 60%) and crucially, the implementation of streamlined initiation on direct acting antiviral therapy (including expedited multidisciplinary team approval and unrestricted pangenotypic treatment) also yielded in a four-fold increase in treatment uptake (85% vs 21%; Fig. 2).

Our results provide more data on HCV epidemiology, indicating that it is not homogenous across the prison population. In our setting, dry blood spot screening might be considered more of a reflection of general prison population prevalence, where 43% of those who test positive were considered to be active people who inject drugs and the chronic HCV prevalence was 2.6%. In comparison, using rapid point-of-care screening the chronic HCV prevalence was 12.3% among those undergoing induction on opioid substitution therapy, where the proportion of active people who inject drugs (defined as injecting drug use within the past year) was much higher (75%). However, the relatively low uptake of opt-out dry blood spot screening hampers the utility of any derived HCV prevalence data and introduces a selection bias, which could mean a certain sub-population being over-or-underrepresented. For example, during our study, only 2 of the 28 HCV seropositive individuals (7%) from rapid point-of-care screening underwent simultaneous dry blood spot testing. Ordinarily, the remainder may have potentially completed their prison stay without being identified. In this study the alternative point-of-care pathway improved the efficiency of both diagnosis and treatment uptake, averting unnecessary costs related to screening in the absence of treatment and disease morbidity. However, a more formal health economic evaluation should be undertaken to truly determine if this intervention is to be considered cost effective.

Despite universal dry blood spot prison screening being considered

Table 3
HCV seroprevalence, confirmation of HCV RNA and chronic HCV prevalence for conventional dry blood spot and alternative point of care screening pathways.

Test	Dry blood spot	Point of care
HCV Ab prevalence, n (%, 95% CI)	91/2442 (3.7, 3.0–4.5)	28/162 (17.3, 11.8–24.0)
HCV RNA performed, n (%, 95% CI)	83/91 (91.2, 85.1–96.8)	24/28 (85.7, 73.2–98.9)
HCV RNA prevalence, n (%, 95% CI)	62/2442 (2.6, 2.0–3.2)	20/162 (12.3, 7.7–18.4)

to be 'opt-out', more than half of the population remains unscreened. Our experience appears to be better than the national prison average for dry blood spot screening (21%), which is likely to be a product of the strong collaboration and enthusiasm of the local clinical and Hepatology teams. In addition, engagement in dry blood spot screening in London prisons appears to be higher than the national average (NHSE London BBV Steering Group, 2019). However, an explanation for a failure to achieve higher uptake is required. A recent multi-center analysis from the UK suggests that the common barriers encountered are related to the prioritization of prison security (limiting the time where an individual may have testing performed) and healthcare inadequacies (including infrastructure and staffing to undertake systematic screening) (Jack, Thomson & Irving, 2019). In addition, completion of screening on arrival into prison is associated with higher uptake and completion of screening (Beckwith et al., 2012). This is particularly relevant to our setting, where there is a delay between offering and completion of dry blood spot testing. Finally, though true refusal rate was not reliably recorded as part of the conventional dry blood spot screening, it was collected in the alternative point-of-care pathway, where only a minority (10%) declined screening. These results are similar to findings of a pilot study at Feltham young offenders' institute, where salivary Oraquick® testing uptake was 100% (Candfield et al., 2017). It is conceivable that as salivary testing is less time consuming, less technically challenging and provides almost immediate results that screening and potential linkage-to-care might be better. However, existing literature also reports excellent acceptability of dry blood spot testing in marginalised populations, indicating that it would be incongruous to conclude that poor dry blood spot uptake in our setting could be explained by patient refusal alone (Abou-Saleh et al., 2008).

The appropriate allocation of trained healthcare staff to undertake the task of dry blood spot screening is also an important factor to consider. It is our understanding that there has been an intensive drive to up-skill prison staff on dry blood spot testing in recent times, however commonly their attention is drawn to focus on other important healthcare needs and thus may deprioritize dry blood spot screening as they may not be fully aware of the tangible benefits available to those who test positive. In contrast, the efficiency of screening was maximized in our rapid alternative point-of-care screening pathway by empowering a dedicated and well-trained healthcare assistant with appropriate knowledge, time and skills to undertake HCV testing.

Another special consideration for our setting is shortening the time taken to transition through the cascade of care. Our HCV-infected prison population are predominantly on remand and typically serve short sentences. The existing guidance recommends that dry blood spot screening is perform within 72 h of inmate arrival, however our study reports that in reality this happens around one week after admission (Public Health England, 2014). Although conventional dry blood spot testing has the added benefit of reflex qualitative HCV PCR and genotyping, this can take up to 3 weeks to be completed and in 8/91(9%) of cases viral confirmation was not performed due to inadequate sample volume or assay failure. Thus, in our setting where most individuals serve short sentences the delays encountered by the time taken to complete dry blood spot-based testing potentially adversely affects adherence to the cascade of care. In comparison, we have demonstrated that the implementation of rapid point-of-care screening in combination with a simplification of the linkage-to-care process has the benefit of significantly reduced the time to diagnosis and improves likelihood of treatment initiation.

Unlike in other countries like Australia (Kirby Institute, 2018), where a more flexible direct acting antiviral prescribing policy exists, the operational delivery network structure in England is yet to relax its requirement for treatment initiation. Despite access to pangenotypic therapies, choice of drug is dictated by genotype, existence of cirrhosis and treatment experience. In addition, operational delivery networks are financially penalized for failing to collect SVR12 data, which in turn disincentivizes physicians to commence treatment on inmates who are likely to be lost to follow up. In our experience of the conventional dry blood spot pathway these factors have yielded unacceptably low rates of clinical assessment, treatment approval and initiation. Currently, very little continuity of care exists in the community, with no integration of HCV treatment strategies within probation services and reports of sub-optimal linkage-to-care in homeless outreach programs (Selvapatt & Brown, 2015). Therefore, it is unsurprising that none of the inmates who were released engaged with our clinical team in the community. Consequently, refining the operational delivery network model in addition to improving collaboration with existing community programs could have a major impact on enhancing treatment uptake in prison settings.

Recently, the EASL International Liver Foundation endorsed the concept of 'micro-elimination', which encourages identifying and addressing population-specific barriers by developing a tailored approach to improve access to HCV care (Lazarus, Wiktor, Colombo, Thursz & Foundation, 2017). A custodial sentence represents a key opportunity to focus on a population that would otherwise be extremely difficult to engage in the community. An added incentive for expanded access to HCV treatment in prison is the potential to reduce in-prison HCV transmission, particularly given the lack of access to harm reduction (including clean injecting equipment) and risk of transmission from other routes (e.g. tattoos) (Zampino, Coppola, Sagnelli, Di Caprio & Sagnelli, 2015). On treatment monitoring of patients in our study (Fig. 3) has shown that the vast majority of patients are rendered aviraemic two weeks into treatment (64%).

We recognize that our study has a number of limitations. Firstly, we present our findings from a single remand prison setting. Although we highlight numerous difficulties, which resonate with a recent systematic review on barriers to accessing HCV care in prison (Vroling et al., 2018), they may not be generalizable to all prison settings in England. Secondly, there are notable differences between the characteristics of the two study populations, which might introduce unintended confounding. For example, the alternative point-of-care pathway had a higher proportion of active people who inject drugs and a better awareness of disease status, which may in-turn have influenced likelihood of engaging in treatment. In addition, the alternative point-of-care pathway was introduced in tandem with conventional dry blood spot screening only among the inmates commencing on opioid substitution therapy, making it potentially easier to conduct in comparison to whole prison screening. Thus, it would be important to assess and compare the alternative point-of-care pathway and conventional dry blood spot screening as part of universal prison population-based testing. Thirdly, although we report the uptake of direct acting antiviral treatment in both screening algorithms, it is likely that the vast majority will be released before the SVR12 timepoint, and despite offering community follow up it is likely that there will be a significant loss to follow up. However, there is reason to be optimistic. A report of a treatment intervention in a New York remand prison setting encountered similar challenges with loss to follow up but reports post-treatment aviraemia of 94% (MacDonald et al., 2017). Finally, though the Xpert® HCV VL Fingerstick assay has been validated for use finger-prick samples (Lamoury et al., 2018), we did not have access to a Xpert® platform onsite and thus processed samples from EDTA stabilized venous blood samples; revealing 100% sensitivity and excellent correlation with laboratory HCV RNA quantification (Supplementary Fig. 1a + b). It will therefore be important to evaluate the acceptability and performance on finger-stick samples with an in-house Xpert® platform in our setting. Nevertheless, we believe that our study provides strong evidence to support the use of point-of-care viral load technology, either as a principle screening test or to confirm chronic infection, coupled with the immediate initiation of treatment in a viraemic individual.

If we were to estimate that 2.6–12.3% of the prison population in England to be chronically infected with HCV, then this would yield

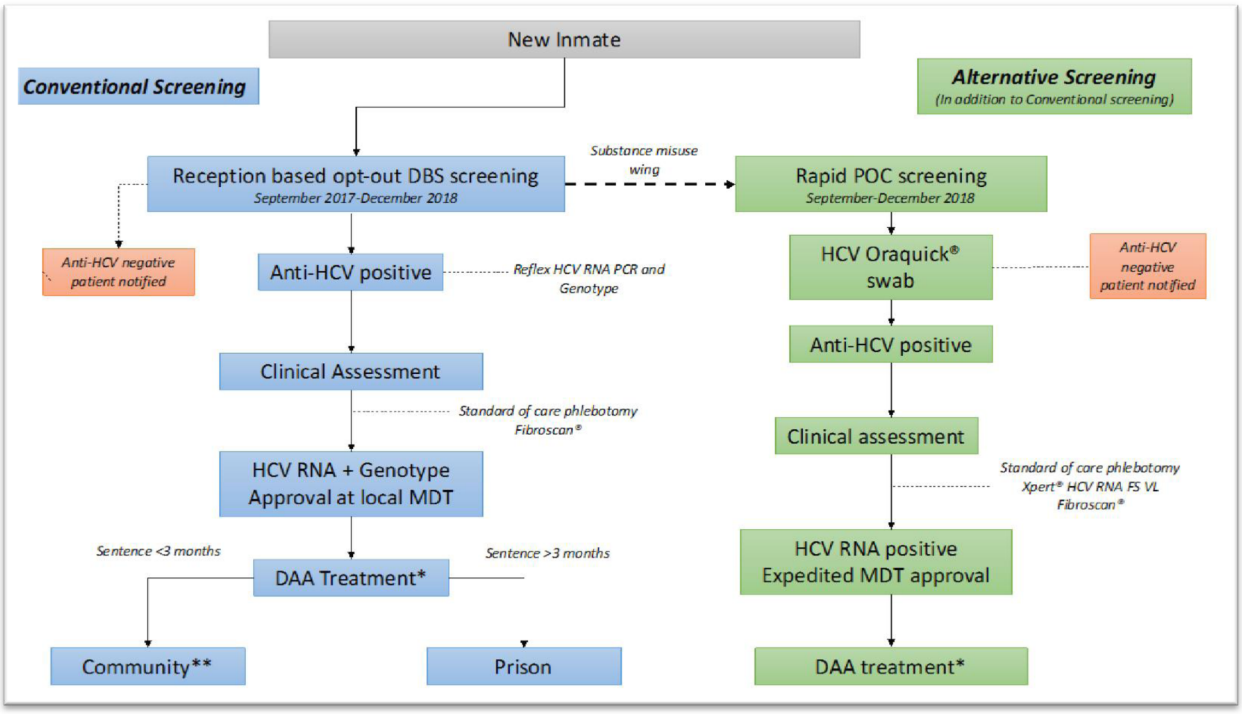

Fig. 1. Summary of conventional dry blood spot and alternative point of care based screening pathways.
*On treatment monitoring 2, 4, end of treatment, 4 and 12 weeks post treatment **Laminated contact card given to patients to initiate treatment on release.

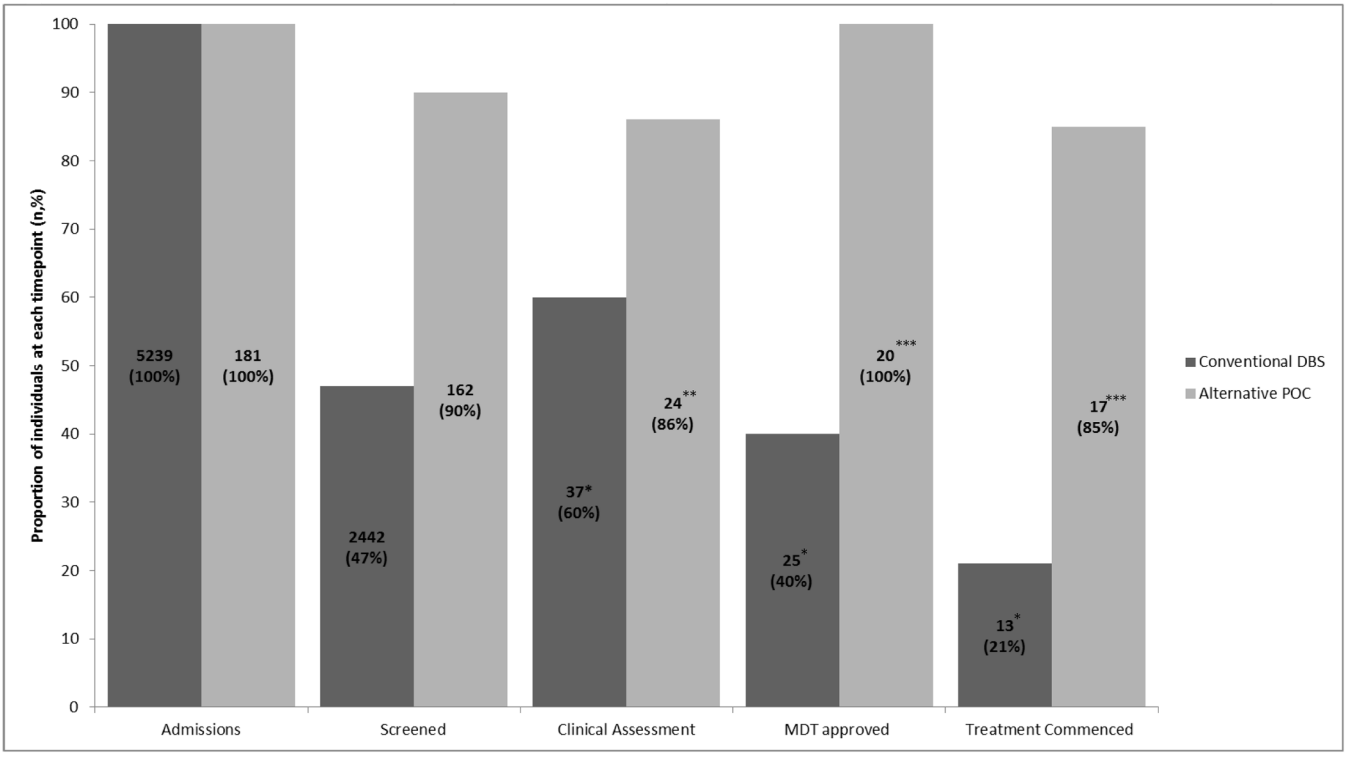

Fig. 2. HCV cascade of care according to conventional dry blood spot or alternative point of care based screening strategy
*Based on proportion of dry blood spot HCV RNA positive patients undergoing clinical assessment, $n = 62$ **Based on proportion of point-of-care HCV anti-HCV antibody positive patients undergoing clinical assessment, $n = 28$ ***Based on proportion of point-of-care HCV RNA positive patients, $n = 20$.

2000–10,000 potential cases requiring treatment. Although we confirm improving efforts at scaling-up HCV diagnosis, through the implementation of dry blood spot screening, uptake remains sub-optimal and subsequent access to treatment is poor. Our implementation of a rapid screening and treatment model successfully combined increased screening coverage with point-of-care diagnostic technology with a simplified linkage-to-care pathway (Fig. 1), which dramatically improved access to treatment. We believe that our model could represent

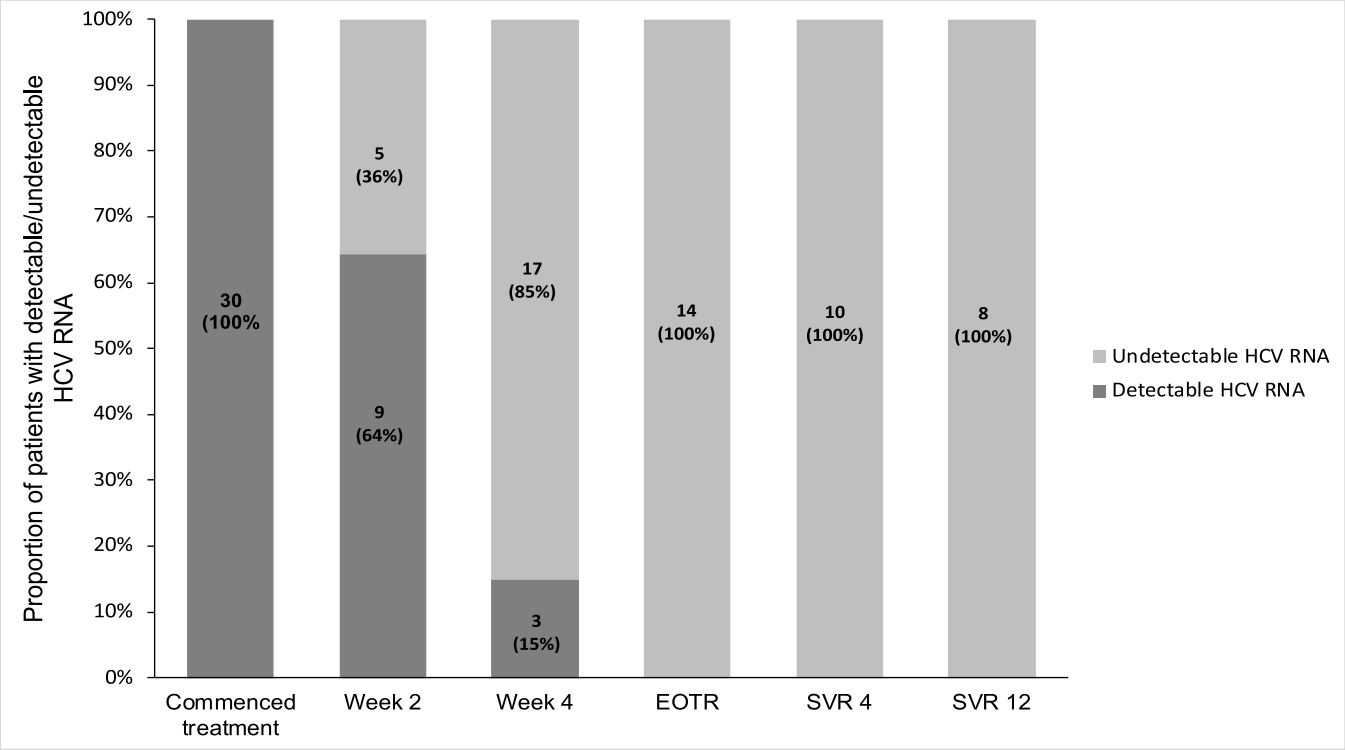

Fig. 3. Proportion of patients from conventional dry blood spot screening with detectable and undetectable HCV RNA during and after antiviral therapy. EOTR; end of treatment response SVR: Sustained virological response (at 4 weeks and 12 week post treatment).

a paradigm shift, particularly in remand settings, which could contribute significantly to HCV micro-elimination in prisons in England and consequently to the wider national HCV elimination agenda.

Declaration of Competing Interest

All authors have no conflict of interest to declare in relation to this study.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.drugpo.2019.102608.

References

Abou-Saleh, M., Davis, P., Rice, P., Checinski, K., Drummond, C., Maxwell, D., et al. (2008). The effectiveness of behavioural interventions in the primary prevention of hepatitis C amongst injecting drug users: A randomised controlled trial and lessons learned. *Harm Reduction Journal, 5*, 25. https://doi.org/10.1186/1477-7517-5-25.

Beckwith, C. G., Nunn, A., Baucom, S., Getachew, A., Akinwumi, A., Herdman, B., et al. (2012). Rapid HIV testing in large urban jails. *American Journal of Public Health, 102*(Suppl 2), S184–S186. https://doi.org/10.2105/AJPH.2011.300514.

Candfield, S., Samuel, M. I., Ritchie, D., McDonald, C., Brady, M., & Taylor, C. (2017). Use and acceptability of salivary hepatitis C virus testing in an english young offender institution. *International Journal of STD & AIDS, 28*(12), 1234–1238. https://doi.org/10.1177/0956462417696214.

Coats, J. T., & Dillon, J. F. (2015). The effect of introducing point-of-care or dried blood spot analysis on the uptake of hepatitis C virus testing in high-risk populations: A systematic review of the literature. *International Journal of Drug Policy, 26*(11), 1050–1055. https://doi.org/10.1016/j.drugpo.2015.05.001.

Cuadrado, A., Llerena, S., Cobo, C., Pallas, J. R., Mateo, M., Cabezas, J., et al. (2018). Microenvironment eradication of hepatitis C: A novel treatment paradigm. *American Journal of Gastroenterology, 113*(11), 1639–1648. https://doi.org/10.1038/s41395-018-0157-x.

Degenhardt, L., Peacock, A., Colledge, S., Leung, J., Grebely, J., Vickerman, P., et al. (2017). Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: A multistage systematic review. *The Lancet. Global health, 5*(12), e1192–e1207. https://doi.org/10.1016/S2214-109X(17)30375-3.

Department of Health. National survey of hepatitis C services in prisons in England. Retrieved fromhttps://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/212817/Hep-C-Prison-Survey.pdf.

Fourati, S., Feld, J. J., Chevaliez, S., & Luhmann, N. (2018). Approaches for simplified HCV diagnostic algorithms. *Journal of the International AIDS Society, 21*(Suppl 2), e25058. https://doi.org/10.1002/jia2.25058.

Grebely, J., Lamoury, F. M. J., Hajarizadeh, B., Mowat, Y., Marshall, A. D., Bajis, S., et al. (2017). Evaluation of the Xpert HCV viral load point-of-care assay from venepuncture-collected and finger-stick capillary whole-blood samples: A cohort study. *The Lancet Gastroenterology and Hepatology, 2*(7), 514–520. https://doi.org/10.1016/S2468-1253(17)30075-4.

Jack, K., Thomson, B. J., & Irving, W. L. (2019). Testing for hepatitis C virus infection in UK prisons: What actually happens. *Journal of Viral Hepatitis, 26*(6), 644–654. https://doi.org/10.1111/jvh.13071.

Kamarulzaman, A., Reid, S. E., Schwitters, A., Wiessing, L., El-Bassel, N., Dolan, K., et al. (2016). Prevention of transmission of HIV, hepatitis B virus, hepatitis C virus, and tuberculosis in prisoners. *Lancet (London, England), 388*(10049), 1115–1126. https://doi.org/10.1016/S0140-6736(16)30769-3.

Kirby Institute. (2018,. July 2018). Monitoring hepatitis C treatment uptake in Australia. Retrieved fromhttps://kirby.unsw.edu.au/sites/default/files/kirby/report/Monitoring-hep-C-treatment-uptake-in-Australia_Iss9-JUL18.pdf.

Kirwan, P., Evans, B. Sentinel Surveillance of Hepatitis Testing Study, G.& Brant, L. . (2011). Hepatitis C and B testing in English prisons is low but increasing. *Journal of Public Health (Oxford, England), 33*(2), 197–204. https://doi.org/10.1093/pubmed/fdr011.

Kronfli, N., Linthwaite, B., Kouyoumdjian, F., Klein, M. B., Lebouche, B., Sebastiani, G., et al. (2018). Interventions to increase testing, linkage to care and treatment of hepatitis C virus (HCV) infection among people in prisons: A systematic review. *International Journal of Drug Policy, 57*, 95–103. https://doi.org/10.1016/j.drugpo.2018.04.003.

Lamoury, F. M. J., Bajis, S., Hajarizadeh, B., Marshall, A. D., Martinello, M., Ivanova, E., et al. (2018). Evaluation of the Xpert HCV viral load finger-stick point-of-care assay. *The Journal of Infectious Diseases, 217*(12), 1889–1896. https://doi.org/10.1093/infdis/jiy114.

Lazarus, J. V., Wiktor, S., Colombo, M., Thursz, M., & Foundation, E. I. L. (2017). Micro-

elimination - A path to global elimination of hepatitis C. *Journal of Hepatology, 67*(4), 665–666. https://doi.org/10.1016/j.jhep.2017.06.033.

MacDonald, R., Akiyama, M. J., Kopolow, A., Rosner, Z., McGahee, W., Joseph, R., et al. (2017). Feasibility of treating Hepatitis C in a transient jail population. *Open Forum Infectious Diseases, 4*(3), https://doi.org/10.1093/ofid/ofx142 ofx142.

Ministry of Justice. prison population figures: (2018). Retrieved fromhttps://www.gov.uk/government/collections/prison-population-statistics.

Morey, S., Hamoodi, A., Jones, D., Young, T., Thompson, C., Dhuny, J., et al. (2019). Increased diagnosis and treatment of hepatitis C in prison by universal offer of testing and use of telemedicine. *Journal of Viral Hepatitis, 26*(1), 101–108. https://doi.org/10.1111/jvh.13017.

NHSE London BBV steering group (2019,. June 2019). [BBV opt-out testing data NHSE London Region].

Papaluca, T., McDonald, L., Craigie, A., Gibson, A., Desmond, P., Wong, D., et al. (2019). Outcomes of treatment for hepatitis C in prisoners using a nurse-led, state-wide model of care. *Journal of Hepatology*. https://doi.org/10.1016/j.jhep.2019.01.012.

Public Health England. (2014). Blood-borne virus opt-out testing in prisons: Preliminary evaluation of pathfinder programme. Retrieved from https://www.gov.uk/government/publications/blood-borne-virus-opt-out-testing-in-prisons-evaluation-of-pathfinder-programme.

Public Health England. (2017a). Hepatitis C in the UK: 2017 report. Retrieved fromhttps://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/632465/HCV_in_the_uk_report_2017.pdf.

Public Health England. (2017b). National engagement event for blood-borne virus (BBV) opt-out testing in prisons in England.

Schito, M., Peter, T. F., Cavanaugh, S., Piatek, A. S., Young, G. J., Alexander, H., et al. (2012). Opportunities and challenges for cost-efficient implementation of new point-of-care diagnostics for HIV and tuberculosis. *The Journal of Infectious Diseases, 205*(Suppl 2), S169–S180. https://doi.org/10.1093/infdis/jis044.

Selvapatt, N., H., L., & Brown, A. S. (2015). PTU-109 a pilot study of outreach testing for hepatitis C and linkage to care in a london centre for homeless persons. *Gut, 64*(A109).

Stone, J., Martin, N. K., Hickman, M., Hutchinson, S. J., Aspinall, E., Taylor, A., et al. (2017). Modelling the impact of incarceration and prison-based hepatitis c virus (HCV) treatment on HCV transmission among people who inject drugs in Scotland. *Addiction, 112*(7), 1302–1314. https://doi.org/10.1111/add.13783.

Taylor, A., Munro, A., Allen, E., Dunleavy, K., Cameron, S., Miller, L., et al. (2013). Low incidence of hepatitis C virus among prisoners in Scotland. *Addiction, 108*(7), 1296–1304. https://doi.org/10.1111/add.12107.

Vroling, H., Oordt-Speets, A. M., Madeddu, G., Babudieri, S., Monarca, R., O'Moore, E., et al. (2018). A systematic review on models of care effectiveness and barriers to Hepatitis C treatment in prison settings in the EU/EEA. *Journal of Viral Hepatitis, 25*(12), 1406–1422. https://doi.org/10.1111/jvh.12998.

Walmsey, R. (2016). World prison population list. 11. Retrieved fromhttp://www.prisonstudies.org/sites/default/files/resources/downloads/world_prison_population_list_11th_edition_0.pdf.

Weild, A. R., Gill, O. N., Bennett, D., Livingstone, S. J., Parry, J. V., & Curran, L. (2000). Prevalence of HIV, hepatitis B, and hepatitis C antibodies in prisoners in england and wales: A national survey. *Communicable Disease and Public Health, 3*(2), 121–126. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/10902255.

World Health Organisation. (2017). WHO prequalification of in vitro diagnostics. Retrieved fromhttps://www.who.int/diagnostics_laboratory/evaluations/pq-list/hcv/170404_final_pq_report_pqdx_0260-070-00.pdf?ua=1.

Zampino, R., Coppola, N., Sagnelli, C., Di Caprio, G., & Sagnelli, E. (2015). Hepatitis C virus infection and prisoners: Epidemiology, outcome and treatment. *World Journal of Hepatology, 7*(21), 2323–2330. https://doi.org/10.4254/wjh.v7.i21.2323.