

# Cost-effectiveness of strategies to improve HCV screening, linkage-to-care and treatment in remand prison settings in England

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## Abstract

**Background:** A simplified cascade-of-care may improve screening and treatment uptake among incarcerated individuals. We assessed the cost-effectiveness of traditional and simplified screening and treatment in a London remand prison.

**Methods:** Using empirical data from Her Majesty's Prison (HMP) Wormwood Scrubs, London, we designed a decision tree and Markov transition state model using national average data for HCV screening and treatment for the base-case scenario. This compared two alternative strategies; (a) general prison population screening and treatment and (b) prioritising screening and treatment among people who inject drugs (PWID) combined with general prison population screening and treatment. Strategies varied the rates of screening (47%-90%), linkage-to-care (60%-86%) and treatment (21%-85%). Cost, utility and disease transition rates were obtained from existing literature. Outcome measures were as follows: screening, treatment and disease-related costs per admitted individual, quality-adjusted life years (QALYs). Incremental cost-effectiveness ratios (ICERs) were calculated for each intervention. All costs and utilities were discounted at a rate of 3.5% per annum. Both univariate and probabilistic sensitivity analyses have been conducted.

**Results:** In our cohort of 5239 incarcerated individuals with an estimated chronic HCV prevalence of 2.6%, all strategy ICER values (£3565-10 300) fell below the national willingness to pay threshold (£30 000). Increased successful treatment (7%-54%) was observed by an optimising cascade-of-care. A robust sensitivity analysis identified treatment cost of, QALY for mild liver disease and probability of completing treatment as important factors that impact the ICER value.

**Conclusion:** In our remand setting, optimising adherence to the cascade-of-care is cost-effective. Where universal screening is not practical, a stratified approach focused on intensive screening and treatment of PWID also results in increased treatment uptake and is highly cost-effective.

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## KEY WORDS

cascade of care, cost effectiveness, hepatitis C (HCV), people who inject drugs (PWID), prison

## 1 | INTRODUCTION

The World Health Organisation (WHO) is committed to the elimination of viral hepatitis as a global health issue by 2030 as outlined in its 2016-2021 global health sector strategy.<sup>1</sup> It is estimated that 8% of the global burden of chronic hepatitis c virus (HCV) infection is concentrated among people who inject drugs (PWID).<sup>2,3</sup> A strong association exists between PWID and incarceration, with lifetime rates reported as high as 90%<sup>4</sup> and, furthermore, up to 15% of people living in detention globally are estimated to be infected with HCV.<sup>5</sup>

Furthermore, recent modelling studies have estimated that PWID are accountable for 79% of HCV transmission and also underlined the value of sustained treatment as prevention with direct-acting antiviral (DAA) therapy in combination with scaling-up harm reduction (HR).<sup>3,6</sup> Thus, it is clear that addressing the HCV epidemic among PWID is a key priority, which will influence the success of global attempts to eliminate HCV. In practice, however, implementing a successful treatment initiative in this marginalised community can prove difficult. For example, a recent prospective evaluation reported less than 10% treatment uptake among newly diagnosed PWID in San Francisco.<sup>7</sup> Therefore, engaging infected individuals serving a custodial sentence has been identified as a potentially opportune circumstance.

Recognising the importance of HCV infection among prison populations, countries including: Australia, China, India, Iran and the USA, have started to include prison programmes for HCV screening and treatment as part of their national hepatitis plans.<sup>8</sup> In England, 'opt-out' dry blood spot (DBS) screening for HCV infection has been phased into the prison estates since 2014.

Mathematical models have estimated that scaling-up prison-based HCV screening, treatment and harm reduction in Scotland will reduce the incidence and prevalence of HCV among PWID by almost half.<sup>9</sup> The use of DBS-based prison HCV screening has been found to be cost-effective only when linkage to care is greater than 40% and is considered highly cost-effective when combined with incrementing levels of treatment using DAA therapy.<sup>10,11</sup> Furthermore, the scale-up of HCV interventions in prison have also been found to be cost-effective in Switzerland and the USA.<sup>12,13</sup>

However, in England, there is clearly room for improvement, as despite having a national opt-out DBS screening policy, existing rates of screening are around 20%, while only a minority of individuals are accessing treatment.<sup>14</sup> We have recently demonstrated that a simplified screening and treatment algorithm, implementing point-of-care screening and streamlined treatment initiation of all viraemic individuals, resulted in screening uptake of 90% and treatment uptake of 85% in prisons.<sup>15</sup> However, no study to date has assessed the cost-effectiveness such a strategy, which simplifies the cascade of care in prisons. Between September 2017 and December 2018 at (Her Majesty's

### LAY SUMMARY

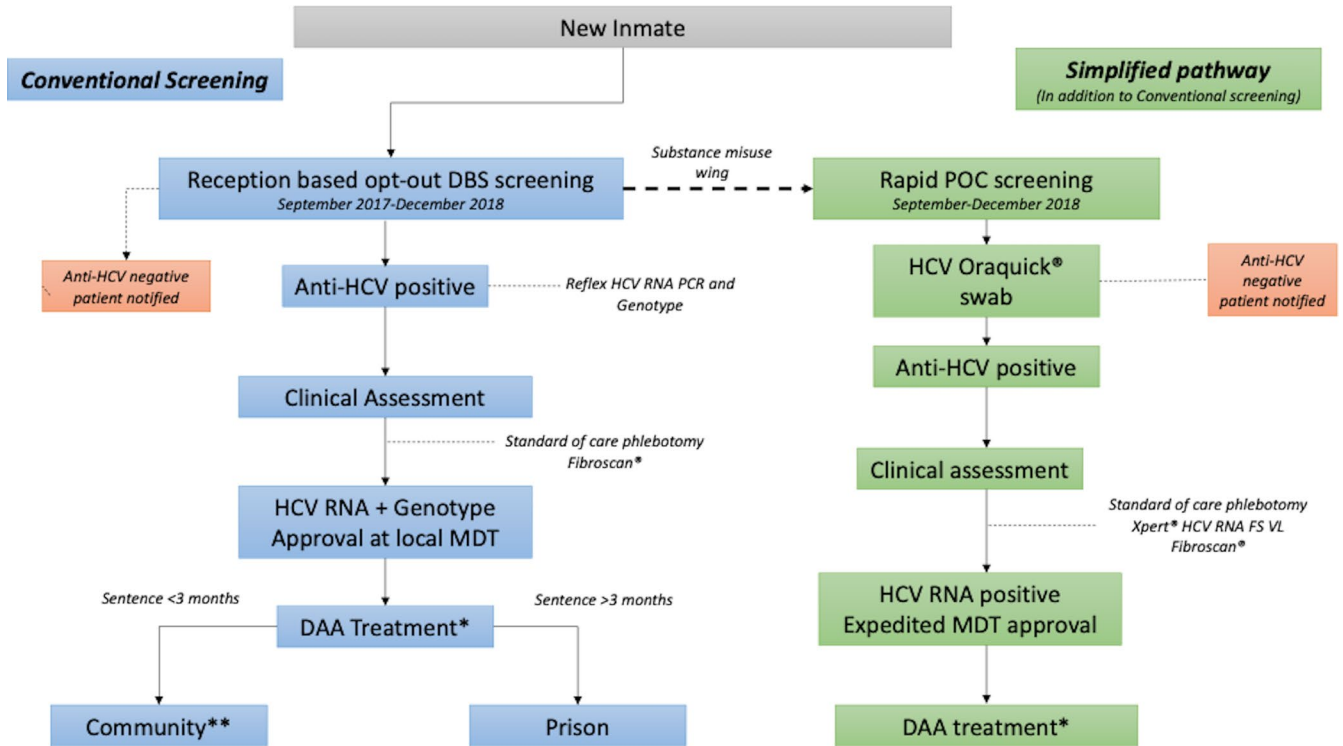
Despite rolling-out a national screening programme for hepatitis C among people in prison in England, rates of screening and treatment remain suboptimal. In remand settings, point-of-care testing and fast-track treatment initiation can improve treatment uptake. In comparison to national average rates, optimising screening, linkage-to-care and treatment is highly cost-effective as both in universal and targeted testing among people who inject drugs in our remand prison settings. These data support the adoption of policies to simplify the testing and treatment practices in prison settings in England.

Prison) HMP Wormwood Scrubs universal opt-out DBS general prison population screening was combined with an in-reach Hepatology clinic and treatment in line with the NHS England approved DAA therapy for patients with a sentence long enough to complete treatment, while those with shorter sentences were provided with contact information for community linkage-to-care. In addition, between September and December 2018 we evaluated a simplified pathway involving point-of-care screening (Oraquick® anti-HCV (Orasure®, Bethlehem, PA) screening followed by Xpert® HCV fingerstick viral load (Xpert® HCV FS VL) (Cepheid®, Sunnyvale, CA) confirmation), fast-track treatment approval and initiation irrespective of sentence duration.<sup>15</sup> A flow diagram summarising both interventions can be found in Figure 1. Using this empirical data on screening and treatment outcomes from HMP Wormwood Scrubs, a medium-security remand prison in West London, we assessed the cost-effectiveness of five strategies, which evaluate a combination of screening (DBS and point-of-care based) and treatment (restricted and unrestricted by length of stay) initiatives.

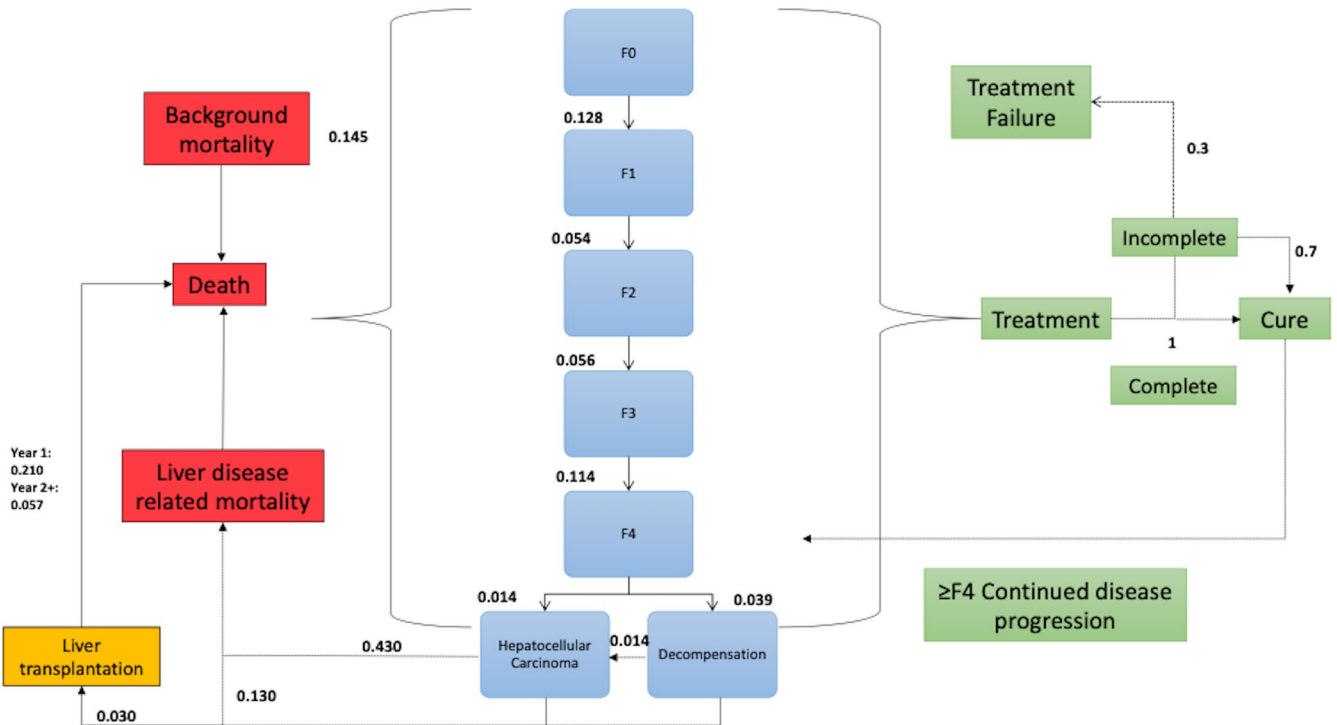
## 2 | METHODS

### 2.1 | Model structure

A de novo closed-cohort decision tree and Markov state transition model was created using TreeagePro® (Williamstown, MA) modelling software to simulate accrued costs and health-related outcomes related to screening and treatment of HCV in our prison setting over a 30-year time horizon. For all strategies a representative cascade of care was integrated to include 4 critical steps; serology screening and active infection confirmation, linkage-to-care (defined as clinical assessment), treatment initiation and sustained virological response at 12 weeks post-therapy (SVR 12).



**FIGURE 1** Summary of universal opt-out general prison population DBS and targeted high-risk simplified pathways implemented at HMP Wormwood Scrubs.<sup>15</sup> \* Patient given contact details to self-refer for treatment in community; \*\* direct acting antiviral treatment



**FIGURE 2** Natural history model and transition probabilities for fibrosis progression, treatment outcomes and associated morbidity and mortality

Figure 2 summarises the model natural history. Liver disease progression from mild (F0/F1) and moderate (F2/3) disease to compensated cirrhosis (F4) and its associated complications

(decompensation (DC) and hepatocellular carcinoma (HCC) was included in the model, parameterised from existing literature.<sup>15-17</sup> Given the high-risk status of the population, it is assumed that the

transmission of disease has occurred as a result of injecting drug use. All successfully treated non-cirrhotic patients experienced a halt in their liver disease progression. Meanwhile all untreated and cirrhotic individuals (irrespective of treatment status) continue to experience disease progression through the model lifespan. In addition to disease-specific morbidity and mortality, a standardised background prisoner mortality rate has been applied to our cohort.<sup>18</sup> The model also assumes a matched background chronic HCV prevalence and disease progression for those who are not retained along the cascade of care.

## 2.2 | Study setting

Where possible, empirical data from both opt-out universal HCV DBS general prison population screening and a pilot simplified screen-and-treat algorithm at HMP Wormwood Scrubs have been used to generate epidemiological, screening and costs parameters.<sup>15</sup> A review of the relevant literature was used to derive all other necessary parameters.

## 2.3 | Interventions

In the following scenarios, we compare varied rates of screening, linkage-to-care and treatment uptake. The status quo scenario (strategy a) used is based on the national average rates of 20% screening and 40% linkage-to-care reported from the health and justice indicators of performance (HJIPs) for 2017-2018.<sup>14</sup> Strategy b reflects the existing HCV cascade of care at HMP Wormwood scrubs, while optimised rates of screening, linkage-to-care and treatment are varied based on data from a pilot 'simplified pathway' (incorporating point-of-care screening (Oraquick® anti-HCV screening followed by viraemia confirmation using Xpert® HCV FS VL assay), fast track

linkage-to-care and unrestricted treatment initiation [irrespective of length of sentence]) in strategies c and d.<sup>15</sup> In addition, strategies e and f are comprised of varied intensity of universal general prison population screening and targeted screening of the high-risk prison population, defined as PWID initiated on OST (estimated to be 14% of the total prison population).<sup>19</sup> A summary of all scenarios is listed below, and the proportion of patients screened, linked-to-care and treated in each case can be found in Table 1.

1. National average reception-based universal general prison population DBS screening (20%), linkage-to-care (40%) and treatment (5%) (Status quo).
2. Local reception-based universal general prison population DBS screening (47%), linkage-to-care (60%) and restricted treatment (21%) of inmates able to complete course in custody (universal DBS).
3. Local reception-based universal general prison population high-uptake DBS screening (90%), linkage-to-care (60%) and restricted treatment (21%) of inmates able to complete course in custody (universal DBS high uptake).
4. Local reception-based universal general prison population simplified pathway (POC screening (90%), expedited linkage-to-care (86%) and unrestricted treatment (85%)) (universal simplified pathway).
5. Stratified screening: Local reception-based universal prison population DBS screening (47%), linkage-to-care (60%) and restricted treatment (21%) and high-risk prison population simplified pathway screening (90%), linkage-to-care (86%) and treatment (85%) (stratified DBS and simplified pathway).
6. Stratified screening: Local reception-based universal prison population high-uptake DBS screening (90%), linkage-to-care (60%) and restricted treatment (21%) and high-risk prison population simplified pathway screening (90%), linkage-to-care (86%) and treatment (85%) (stratified DBS high uptake and simplified).

**TABLE 1** Base-case cascade of care summaries for each scenario

	Description	Screening uptake (%)	HCV RNA prevalence (%)	Linkage to care (%)	Treatment uptake (%)	Sustained virological response (%)
National Average	(a) Status Quo	20	2.6	40	5	100
Universal Screening: general prison population	(b) DBS screening	47	2.6	60	21	100
	(c) High-uptake DBS screening	90	2.6	60	21	100
	(d) Simplified pathway	90	2.6	86	85	100/70 <sup>b</sup>
Stratified Screening (universal vs high-risk prison population)	(e) Universal DBS screening + Simplified pathway high risk	47/90	1.1/12.5 <sup>a</sup>	60/86	21/85	100/70 <sup>b</sup>
	(f) Universal high-uptake DBS screening + Simplified pathway high risk	90/90	1.1/12.5 <sup>a</sup>	60/86	21/85	100/70 <sup>b</sup>

<sup>a</sup>General prison population value adjusted to maintain overall HCV RNA prevalence at 2.6%.

<sup>b</sup>Completed treatment SVR = 100%, Incomplete treatment SVR = 70%.

## 2.4 | Costing

Costs were considered from a healthcare provider perspective. The total assay cost for screening using DBS was £179.91 (£9.91 anti-HCV,<sup>14</sup> £100 DBS HCV RNA and genotype and £70 laboratory HCV RNA and genotype validation<sup>15</sup>). While the cost of POC in the simplified algorithm was £117 (Oraquick® anti-HCV; £17, Xpert® HCV FS VL; £30 and laboratory HCV RNA and genotype validation; £70<sup>15</sup>). The cost of clinical assessment was £225 (Fibroscan®; £150 and healthcare professional time; £125<sup>15</sup>) and the total cost of treatment and follow-up was £10 500 (DAA therapy; £10 000, healthcare professional time; £500). HCV disease-related costs were derived from existing literature.<sup>20,21</sup> The costs related to each scenario are presented per capita offered testing as opposed to per capita screened as this allowed us to take into account a health-related output costs among the estimated proportion of individuals who did not undergo screening.

## 2.5 | Outcome measures

Quality-adjusted life years (QALYs) were used to as an quantitative objective measure of HCV-related disease morbidity and each stage of liver disease (mild, moderate, cirrhosis, decompensation and HCC) and liver transplantation (at 1 year post-transplantation and long term) was assigned a value based on existing literature.<sup>20,21</sup> An incremental QALY was applied for non-cirrhotic prisoners who completed therapy successfully.<sup>11</sup>

## 2.6 | Cost-effectiveness

Using the status quo scenario as the base case, an incremental cost-effectiveness ratio (ICER) per QALY gained for each alternative strategy was generated using the following formula:

$$\frac{(\text{Cost}_{\text{strategy b} - \text{j}} - \text{Cost}_{\text{strategy a}})}{(\text{Effectiveness}_{\text{strategy b} - \text{j}} - \text{Effectiveness}_{\text{strategy a}})}$$

A half-cycle correction was applied to all recurrent costs and health utilities. This methodology is commonly applied in Markov modelling.<sup>22</sup> In the model the transition from one state to another is discrete (occurring at the beginning or end of a cycle), however, in reality this process is likely to be continuous throughout the cycle. Half of the total accrued costs and effects are taken for the first and last cycle, effectively resulting in the estimate for all intermediate cycles being obtained from the middle time point, avoiding over- or under-estimation of the incurred outputs associated with the transition between states.<sup>23</sup> In addition, a standardised discount was applied to all outputs at a rate of 3.5% per annum. In line with the UK National Institute of Health and Care Excellence (NICE), the willingness to pay threshold (WTP) used to assess whether a strategy was cost-effective or not was considered to be £20 000 to £30 000 per QALY gained.<sup>24</sup>

## 2.7 | Sensitivity analysis

In order to evaluate the robustness of the results generated, both deterministic (univariate) analysis and probabilistic sensitivity analysis (PSA) have been performed for cost, health utility and probability parameters (Table 2). For deterministic analysis a range of parameter values were tested for each variable evaluated, while Monte Carlo Simulation was used to generate 1000 randomised simulations for PSA.

## 3 | RESULTS

### 3.1 | Impact of treatment on HCV disease progression and related mortality

Table 3. and Figure S3A,B. summarise the difference in disease state for both treated and untreated groups over the 30-year model span. At baseline 78% of patients had mild disease (F0/F1), 11% had moderate disease (F2/F3), 11% have compensated cirrhosis (F4) and none had any associated complication (DC or HCC). There was a significant change in the profile of early liver disease when comparing treated with untreated and unsuccessfully treated cases. The majority of successfully treated individuals remained in the mild disease state (F0/1) (70.7%). In comparison, 19.0% of untreated and unsuccessfully treated individuals remained in the mild disease state, while the majority had progressed to the moderate disease state (57.2%) after 30 years. There were less pronounced differences in the proportion of advanced liver disease between groups. Levels of compensated cirrhosis (3.4% vs 1.9%) and DC (1.0% vs 0.6%) were lower among treated individuals, while the proportion with HCC was equivalent in both groups (0.1%). Finally, overall mortality was lower among treated individuals (16.7% vs 19.1%).

### 3.2 | Cost-effectiveness analysis

Between September 2017 and December 2018, 5239 individuals were admitted to HMP Wormwood Scrubs, based on existing literature it is estimated that 14% (733 inmates) were initiated on OST.<sup>19</sup> In comparison to the base case (strategy a), over the course of 30-year model timeframe, the greatest per capita total cost (testing, morbidity related and treatment) difference observed was £205 (strategy d; universal simplified pathway), while the greatest per capita margin in health utility was 0.02 QALYs (strategies D (universal simplified pathway) and F (stratified universal high-uptake DBS screening and high-risk simplified pathway).

The results of the cost-effectiveness analysis are presented in Table 4. All five strategies reported an ICER which fell below the WTP threshold for the UK (£20 000 to 30 000), with ICER per QALY gained values ranging from £3402 (strategy b; universal DBS screening) to £10 300 (strategy c; universal high-uptake DBS screening).

**TABLE 2** List of input variable mean and distribution values for cost, utility and probability

Parameter	Mean Value	Distribution	Source/ Remarks
<b>Cost (£)</b>			
Cost of DBS HCV antibody screen	9.91	Uniform $\pm$ 20%	26
Cost of DBS HCV RNA/Genotype	170.00	Uniform (100-204)	15
Cost of Orasure HCV antibody screen	17.00	Uniform $\pm$ 20%	15
Cost of Xpert® FS HCV RNA	100.00	Uniform (30-120)	15
Cost of clinical assessment	225.00	Uniform $\pm$ 20%	15
Cost of DAA treatment (8-12 weeks)	10 000.00	Uniform (1000-30 000)	
Cost of follow-up	500.00	Uniform $\pm$ 20%	15
Cost Mild disease (F0/1)	177.47	Uniform $\pm$ 20%	20,21
Cost Moderate disease (F2/3)	922.08	Uniform $\pm$ 20%	20,21
Cost Compensated cirrhosis (F4)	1463.50	Uniform $\pm$ 20%	20,21
Cost Decompensated Cirrhosis	11 728.61	Uniform $\pm$ 20%	20,21
Cost Hepatocellular Carcinoma	10 451.58	Uniform $\pm$ 20%	20
Cost Liver transplant	47 310.55	Uniform $\pm$ 20%	20
Cost post liver transplant	1781.15	Uniform $\pm$ 20%	20
Cost Mild disease SVR	333.08	Uniform $\pm$ 20%	20
Cost Moderate disease SVR	922.08	Uniform $\pm$ 20%	20
Cost Compensated cirrhosis SVR	1463.50	Uniform $\pm$ 20%	20
<b>Health Utility (QALYs)</b>			
Uninfected/Spontaneous Clearance	0.94	Uniform $\pm$ 20%	11
Background prisoner mortality rate	0.0033	Uniform - 20% to 1.14 per 100 person-years	18,33
Mild disease (F0/1)	0.77	Beta ( $\alpha = 769.23, \beta = 229.77$ )	20,21
Moderate disease (F2/3)	0.66	Beta ( $\alpha = 659.34, \beta = 339.65$ )	20,21
Compensated cirrhosis (F4)	0.55	Beta ( $\alpha = 549.45, \beta = 449.55$ )	20,21
Decompensated cirrhosis	0.45	Beta ( $\alpha = 449.54, \beta = 549.45$ )	20,21
Hepatocellular Cancer	0.45	Beta ( $\alpha = 449.54, \beta = 549.45$ )	20,21
Liver transplant	0.45	Beta ( $\alpha = 449.54, \beta = 549.45$ )	20,21
Post liver transplant	0.67	Beta ( $\alpha = 669.33, \beta = 329.67$ )	34
Mild disease SVR	0.82	Beta ( $\alpha = 819.17, \beta = 179.82$ )	20,21
Moderate disease SVR	0.72	Beta ( $\alpha = 719.28, \beta = 329.67$ )	20,21
Compensated cirrhosis SVR	0.61	Beta ( $\alpha = 669.33, \beta = 179.82$ )	34
<b>Probabilities</b>			
F0	0.66	-	15
F1	0.12	-	15
F2	0.06	-	15
F3	0.05	-	15
F4	0.11	-	15
F0-F1	0.128	Uniform $\pm$ 20%	17
F1-F2	0.059	Uniform $\pm$ 20%	17
F2-F3	0.056	Uniform $\pm$ 20%	17
F3-F4	0.116	Uniform $\pm$ 20%	17
Compensated cirrhosis to decompensated cirrhosis	0.039	Uniform $\pm$ 20%	17
Compensated cirrhosis to hepatocellular carcinoma	0.014	Beta ( $\alpha = 38.96, \beta = 960.04$ )	17
Decompensated cirrhosis to hepatocellular cancer	0.014	Beta ( $\alpha = 38.96, \beta = 960.04$ )	17

(Continues)

TABLE 2 (Continued)

Parameter	Mean Value	Distribution	Source/ Remarks
Decompensated cirrhosis/ Hepatocellular cancer to liver transplant	0.030	( $\alpha = 29.97, \beta = 985.01$ )	20
Decompensated cirrhosis to death	0.130	( $\alpha = 129.87, \beta = 869.13$ )	20
Hepatocellular cancer to death	0.430	( $\alpha = 429.57, \beta = 569.43$ )	20
General population chronic prevalence (%)	2.6	Uniform (1.0-8.0)	15
High-risk chronic HCV prevalence (%)	12.5	Uniform (2.6-30.0)	15
Proportion on OST (%)	14	Uniform $\pm$ 20%	15
DBS test performed (%)	47	Uniform 25-100	15
DBS clinical assessment (%)	60	Uniform $\pm$ 20%	15
DBS treated (%)	21	Uniform (5-100)	15
POC test performed (%)	90	Uniform (50-100)	15
POC clinical assessment (%)	85	Uniform (65-100)	15
POC treated (%)	85	Uniform (21-100)	15
POC completed treatment (%)	46	Uniform (37-55)	15
Discounting (%)	3.5	0-7	
Model length (years)	30	15-60	

Disease State	Time point: Baseline All patients (%) <sup>a</sup>	Time point: Year 30	
		Untreated (%)	Successful DAA therapy (%)
Mild Disease (F0/1)	78.0	19.0	70.7
Moderate Disease (F2/3)	11.0	57.2	9.9
Compensated Cirrhosis (F4)	11.0	3.4	1.9
Decompensated Cirrhosis	0	1.0	0.6
Hepatocellular Cancer	0	0.1	0.1
Liver transplant	0	0.2	0.1
Death	0	19.1	16.7

<sup>a</sup>At baseline all patients are considered to be untreated

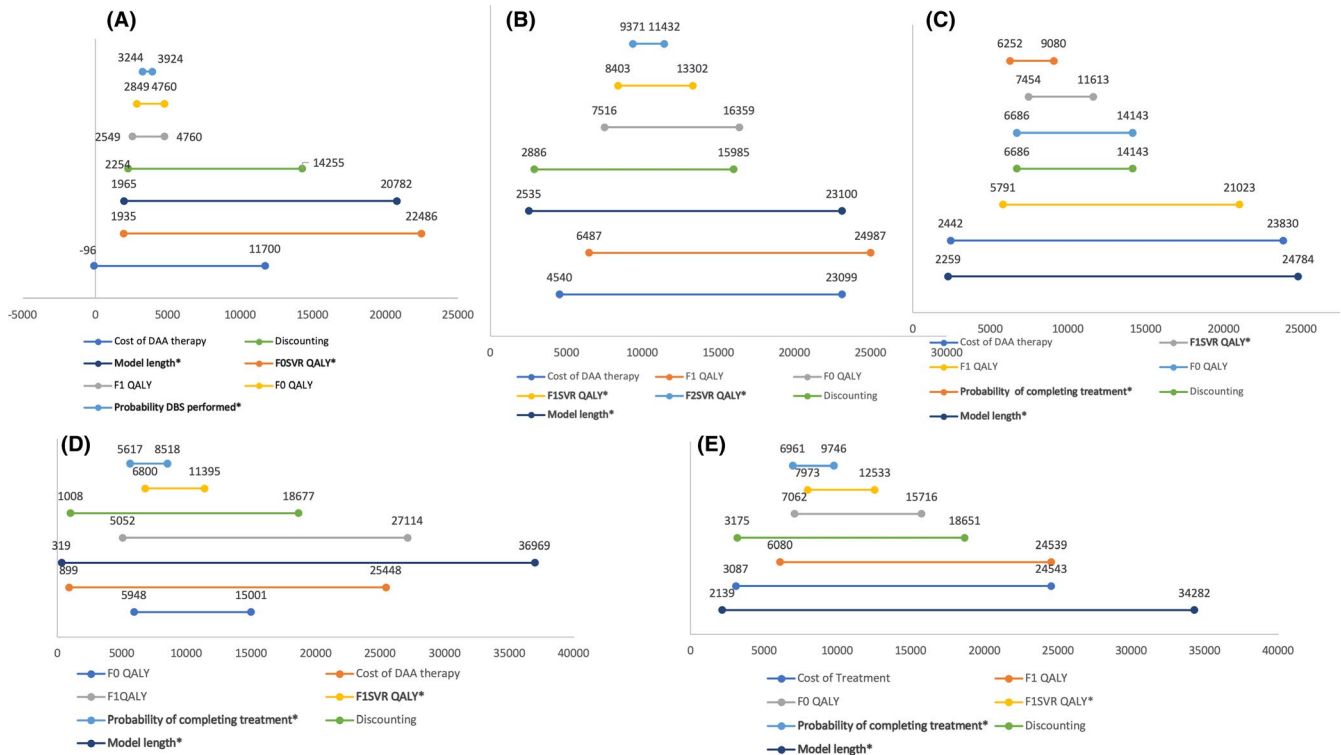
TABLE 3 Comparison of disease liver disease burden and mortality at baseline and at the 30 years post-baseline for both untreated and treated individuals within the cohort

### 3.3 | Sensitivity analysis

The outcomes for the five parameters with the largest impact on the ICER per QALY when compared to the status quo (strategy a) are presented in Figure 3. In all cases none of the parameters appear to independently raise the ICER value above the WTP of £30 000. However, the WTP threshold is breached across all strategies at a more conservative WTP (£20 000). In particular, three common parameters, cost of DDA therapy, the QALY associated with mild disease (F0/1) and the probability of completing

treatment, appear to have the largest effect on the ICER value across all strategies.

Figures S1 and S2 represent outputs from the PSA Monte Carlo simulation. Figure S1 represents a cost-effectiveness acceptability curve, reporting the proportion of simulations for each strategy where the ICER value is considered to be the optimal choice based on an incrementing WTP. Strategy f (stratified DBS high uptake and simplified pathway) becomes the dominant strategy once the WTP exceeds £18 000 and is cost-effective in 73.1% of iterations at a WTP of £30 000.



**FIGURE 3** Outcomes of univariate sensitivity analysis comparing Scenario a (National DBS status quo) to: (A) Universal general prison population DBS, (B) Universal general prison population DBS high uptake, (C) Universal general population simplified pathway, (D) Stratified screening: Universal general prison population: High-uptake DBS screening/High-risk simplified pathway, (E) Stratified screening: Universal general prison population: DBS screening/High-risk simplified pathway. \* Inverse association with ICER value; *Parameters highlighted in bold cross the WTP threshold*

## 4 | DISCUSSION

Our study has shown that all of the evaluated strategies to increase coverage of HCV testing and treatment at HMP Wormwood Scrubs are cost-effective, compared to current national average outcomes for prison-based HCV initiatives in England. The ICERs ranged between £3402 (strategy b) and £10 300 (strategy c), while the net increase in annual cost ranged from £2794 (strategy b) to £35 800 (strategy d) and the proportion of inmates successfully being treated ranged between 7.4% (strategy b) and 53.6% strategy d.

One key message that our model emphasises is the importance of increasing retention along all parts of the cascade of care. This point is emphatically illustrated when increasing screening uptake from 47% strategy b (universal DBS screening) to 90% in strategy c (universal high-uptake DBS) without increase in any other aspect of the cascade of care. This approach results in an almost three-fold increase in cost incurred with only a marginal increase in treatment uptake (7.4% vs 11.0%), reinforcing conclusions made by Martin and colleagues that a combination of increased screening and linkage-to-care is required for a strategy to be cost-effective in England.<sup>11</sup> Until recently the focus of prison-based HCV initiatives has been on increasing the level of testing.<sup>25</sup> However, there is a real danger that the prospective benefit of intensifying screening may be significantly diluted without a reliable pathway to ensure linkage-to-treatment.

A special consideration for our cohort is that it is a remand prison setting where individuals tend to have relatively short sentences, making the cascade of care time sensitive. A major strength of this model is that it was based on empirical data comparing universal DBS-based screening with a point-of-care-based simplified screen-and-treat pathway among PWID initiating on OST at HMP Wormwood Scrubs, making it more representative of the cohort and existing screening practices.<sup>15</sup> We found that a major limitation of DBS screening in this environment is the lag between screening and diagnosis, which often jeopardises intended treatment. Thus, implementing point-of-care testing enables same day diagnosis and, in combination with streamlined treatment initiation, results in optimised adherence to the cascade of care.<sup>15</sup> In this model we have applied these optimised conditions to universal general prison population-based screening (strategy d), which yielded a favourable ICER value (£9080) and the highest number of individuals undergoing successful DAA treatment (73 individuals, 53.6%). These findings are supported by recent cost-effectiveness modelling data from the USA, which compares a wide variety of prison HCV screening and treatment interventions including stratification of screening based on risk status.<sup>13</sup> It also aligns with current national prison screening policy on blood-borne viruses, which advocates untargeted general population screening.<sup>26</sup>

Although it may be preferable to adopt universal HCV screening in prison settings in England, existing clinical and security priorities,



**TABLE 4** Treatment uptake and cost-effectiveness outcomes for each scenario

Scenario	Total treated (n,%) <sup>a</sup>	Total treatment success (n,%) <sup>a</sup>	Total cost per person incarcerated (£)	QALY per person incarcerated	ICER value (£/QALY gain)
(a) National Average	0	0	380	1.22	-
(b) Universal general prison population: DBS screening	10 (7.4)	10 (7.4)	396	1.23	3402.87
(c) Universal general prison population: high-uptake DBS Screening	15 (11.0)	15 (11.0)	426	1.23	10 300.16
(d) Universal general prison population: Simplified pathway	89 (65.4)	73 (53.7)	585	1.25	9080.10
(e) Stratified screening: Universal general prison population: DBS screening/High-risk simplified pathway	63 (46.3)	52 (38.2)	502	1.24	8630.62
(f) Stratified screening: Universal general prison population: High-uptake DBS screening/High-risk simplified pathway	63 (46.3)	52 (38.2)	542	1.24	9745.82

<sup>a</sup>Total number of viraemic individuals calculated as 2.6% of 5239 (136).

combined with a lack of healthcare personnel, can present significant obstacles to its implementation.<sup>27</sup> Thus, in our model we explored the cost-effectiveness of an 'imperfect' intervention by implementing the simplified pathway among PWID being initiated on OST, while continuing either existing (47%) or enhanced (90%) levels of DBS screening without improvement in linkage-to-care or treatment (strategies E and F). Both strategies yielded an ICER value similar to strategy d (strategy e; £8630 and strategy f; £9745) and slightly lower treatment uptake (52 individuals (38.2%)). Enhanced screening among PWID not only has the added benefits of a higher yield, as there is a five-fold increase in chronic HCV prevalence compared to the general prison population, but also may be easier to sustainably implement, given that on average approximately 14% of the total prison population are initiated on OST. In addition, we have demonstrated that while assessing the simplified pathway among those initiated on OST only 7% underwent conventional opt-out DBS screening as part of their admission, despite the initiatives being run in tandem.<sup>15</sup> It is therefore conceivable that reducing the proportion of unscreened high-risk individuals may increase the total number of cases identified.

In order to test the robustness of the cost-effectiveness analysis outputs from our model, a rigorous sensitivity analysis has been performed. Altering the model length and the percentage discounting to the model outputs appear to both have a wide-ranging effect on the ICER values generated. Specifically, when the model length is halved (to 15 years), the ICER value breaches the £30 000 WTP threshold in the strategies where screening and treatment is scaled-up (strategies d-f) (Table 4). This is a consequence of incurring the upfront costs of screening, while the impact of limiting disease progression has yet to be gained. Conversely, removing

any discount to model outputs or increasing the length of the model further results in a more cost-effective ICER across strategies (Figure 3). In terms of cost, the price of treatment has the most significant effect of the ICER values for all scenarios tested. This is in line with an economic evaluation of scaling-up HCV treatment in prisons in the USA, which forecasts that the most significant cost to the healthcare budget within the prison system would be the cost of treatment.<sup>28</sup> In our study we selected a relatively conservative estimate for DAA therapy of £10 000. However, in recent times, NHS England and the pharmaceutical industry have agreed to significant reductions on drug tariffs, and it can only be expected that these costs will continue to fall.<sup>29</sup>

In addition to the cost of therapy, the successful completion of treatment is an important consideration in the sensitivity analysis. As a result of the limited length of incarceration, in our experience only 46% of individuals complete treatment under supervision. We have applied a sub-optimal SVR rate (70%) to those who are released prior to completing therapy. Although, recent work to assess the sub-optimal adherence among PWID concluded that there was no observed difference compared to those with better compliance, this was defined as adherence of less than 90%,<sup>30</sup> whereas it is expected to be around 50% in our cohort. Currently there is very little continuity of HCV care with probation services and community harm reduction programmes on release. Thus, improved collaboration with community services to ensure adequate support for individuals to complete therapy would further enhance the cost-effectiveness of prison-based screening and treatment.

It is also interesting to note the impact of treatment in preventing the morbidity and mortality related to liver disease in this cohort.

The most alarming finding is the high level of mortality observed despite the relatively mild degree of liver disease in the study cohort at baseline. Even after suspending the contribution of background mortality on the model, the proportion who die over a 30-year period is 3.7% higher among those who are untreated (8.0% vs 10.7%). These findings are echoed in a recent analysis of mortality in an observational cohort of over 100 000 HCV infected non-cirrhotic individuals, reporting a hazard ratio of 0.32 among those successfully treated with DAA therapy compared with untreated individuals.<sup>31</sup> The gain in health-related quality of life from treatment also appears to be an important determinant of the ICER value across all strategies, particularly in the cohort with 'mild disease' (F0/1). This is because the averted progression of more advanced disease states in those undergoing treatment. A 20 per cent adjustment in the QALY value for treated and untreated individuals with mild disease resulted in an ICER per QALY gained between £20 000 and £30 000 in the more intensive screening and treatment strategies (Figure 3). This suggests that even where there is no direct health benefit of treatment on an individual level, there is still a cohort benefit at a cost that is likely to be acceptable at the current threshold.

We do acknowledge that there are some limitations to our study. Firstly, our data are generated from a single remand prison site in London. Although this population typically serve short sentences and are therefore theoretically more difficult to treat, the make-up of the prison population, model of treatment delivery and allocation of staff and resources across England is not uniform and therefore our findings need to be generalised with caution. Secondly, we have made the assumption that the fibrosis transition rates are the same for both PWID and non-PWID. Although the majority of cases can be attributed to PWID, other modes of transmission (prison tattoos, immigrants from high prevalence countries) exist in this setting and these individuals may have a slower rate of disease progression.<sup>16,32</sup> However, altering the rate of progression in our sensitivity analysis does not seem to significantly affect the cost-effectiveness. Thirdly, our study design also does not account for individuals who may be tested or treated subsequently in the community. However, we acknowledge that continuity of care for individuals being released without completing treatment remains inadequate by adjusting the SVR rate to 70%. Finally, our model is designed as a closed cohort, and as such does not account for any dynamic changes in disease incidence. Thus, any beneficial effects of treatment as prevention is not captured and the role of re-infection is not considered. This concept maybe particularly pertinent to the prison setting in England, as needle-and-syringe services are not available. Therefore, scaling-up treatment en masse may prevent onward HCV transmission where high-risk injecting practices and tattooing may take place and therefore in practice be even more cost-effective than our study has found. Indeed, our data have demonstrated more than two-thirds of individuals are aviraemic 2 weeks into treatment.<sup>15</sup> Thus, it will be of interest to explore the effects treatment as prevention and re-infection in this setting with a dedicated dynamic transmission model.

Short sentences pose a particular challenge to retention along the cascade of care in remand prison settings. Using empirical data for both DBS-based and simplified point-of-care-based interventions at HMP Wormwood Scrubs, we confirm that approaches to improve both HCV screening and linkage-to-treatment are cost-effective when compared to the national average. Enhanced point-of-care screening and unrestricted treatment of PWID may provide a pragmatic and cost-effective approach in a time-and-resource-limited environment. These findings may help to inform future practice and policy on this important subject.

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## CONFLICT OF INTERESTS

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

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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