Ward, Z., Reynolds, R. A., Campbell, L., Martin, N. K., Harrison, G., Irving, W., Hickman, M., & Vickerman, P. (2020). Cost-effectiveness of the HepCATT intervention in specialist drug clinics to improve case-finding and engagement with HCV treatment for people who inject drugs in England. *Addiction*. https://doi.org/10.1111/add.14978

Cost-effectiveness of the HepCATT intervention in specialist drug clinics to improve case-finding and engagement with HCV treatment for people who inject drugs in England

Running head: Cost-effectiveness of HepCATT intervention

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Funding: UK Department of Health, National Institute of Health Research

Conflict of interest disclosure: MH reports personal fees from Gilead, Abbvie, and MSD. PV has received unrestricted research grants from Gilead and honoraria from Gilead and Abbvie. NKM has received unrestricted research grants and honoraria from Gilead and Merck. The other authors declared no conflicts of interest.

Word count: 3691

Abstract

Background and Aims: People who inject drugs (PWID) are at high risk of Hepatitis C virus (HCV) infection; however ~50% are undiagnosed in England and linkage-to-care is poor. This study investigated the cost-effectiveness of an intervention (HepCATT) to improve case-finding and referral to HCV treatment compared with standard-of-care pathways in drug treatment centres (DTCs) in England.

Design: HCV transmission and disease progression model with cost-effectiveness analysis using a health-care perspective. Primary outcome and cost data from the HepCATT study parameterised the intervention, suggesting HepCATT increased HCV testing in DTCs 2.5-fold and engagement onto the HCV treatment pathway 10-fold. Model was used to estimate the decrease in HCV infections and HCV-related deaths from 2016, with costs and health benefits (quality-adjusted life-years or QALYs) tracked over 50 years. Univariable and probabilistic sensitivity analyses (PSA) were undertaken.

Setting: England specific epidemic with 40% prevalence of chronic HCV among PWID.

Participants: PWID attending DTCs.

Intervention: Nurse facilitator in DTCs to improve the HCV care pathway from HCV case-finding to referral and linkage to specialist care. Comparator was the standard-of-care HCV care pathway.

Measurements: Incremental cost-effectiveness ratio (ICER) in terms of cost per QALY gained through improved case-finding.

Findings: Over 50-years per 1000 PWID, the HepCATT intervention could prevent 75 (95% central interval 37-129) deaths and 1,330 (827-2,040) or 51% (30-67%) of all new infections. The mean ICER was £7,986 per QALY gained, with all PSA simulations being cost-effective at a £20,000 per QALY willingness-to-pay threshold. Univariable sensitivity analyses suggest the intervention would become cost-saving if the cost of HCV treatment reduces to £3,900. If scaled up to all PWID in England, the intervention would cost £8.8 million and decrease incidence by 56% (33-70%) by 2030.

Conclusions: Increasing Hepatitis C virus (HCV) infection case-finding and treatment referral in drug treatment centres could be a highly cost-effective strategy for decreasing HCV incidence among people who inject drugs.

Keywords: Hepatitis C virus, people who inject drugs, case-finding, cost-effectiveness

Introduction

Globally, infection with hepatitis C Virus (HCV) infection causes considerable morbidity(1). Injecting drug use is the critical exposure in most developed countries(2). In the UK, people who inject drugs (PWID) account for 90% of new reported cases(3). HCV can now be easily cured with highly effective direct acting antiviral treatments (DAAs)(4), motivating the World Health Organisation (WHO) to set targets for eliminating HCV as a public health threat by 2030(5, 6). The UK has adopted these targets(6) and has recently agreed an elimination tender with pharmaceutical companies to enable this(7). However, low diagnosis and linkage-to-care rates for PWID remain a key barrier to achieving these elimination targets in the UK and globally(3, 8).

UK guidance recommends undertaking case-finding in specialist drug clinics(9, 10) where a high yield of infection can be achieved(11). However, over 2005-2014, only 10% of cases identified in drug treatment centres were treated within a year, highlighting the need to improve the linkage-to-treatment in these settings. There are few studies investigating the cost-effectiveness of such interventions(9, 12, 13), most from the pre-DAA era. The Hepatitis C Awareness Through to Treatment study (HepCATT) showed that a nurse facilitator within drug treatment centres in three English settings could improve the HCV care pathway from HCV case-finding, referral and linkage to specialist care(14). In this paper, we assess the cost-effectiveness of the HepCATT intervention compared to standard-of-care levels of testing and treatment amongst PWID in England. Insights from this analysis will be important for advocating for the further expansion of community-based case-finding and linkage-to-treatment interventions in the UK, some of which now include community-based treatment(15-18).

Methods

The cost-effectiveness analysis compared the costs and impact of increased testing and engagement achieved among PWID through the HepCATT study in drug treatment centres to a counterfactual where the current standard-of-care levels of testing and engagement continues (status quo). The analysis was undertaken from a UK National Health Service (NHS) and Personal Social Services perspective, following National Institute for Health and Care Excellence (NICE) guidelines over a 50-year time horizon(19). Personal Social Services include services not normally covered by the NHS(20), including drug treatment services and the HepCATT intervention being evaluated in this analysis. The analysis incorporated health benefits of preventing long-term disease sequelae among individuals treated for HCV infection and onward transmission prevention benefits for other PWID. Costs (2018 GB pounds) and health utilities (quality-adjusted life years or QALYs) were attached to each disease stage, each discounted at 3.5% per year. The analysis follows broad best practise in clearly describing all details of the modelling, giving details of the derivation of all model parameters, calibrating and validating the model against available data, and incorporating parameter uncertainty(21, 22). The analysis did not follow a pre-registered analysis plan but used similar methods to our previous studies(9, 23).

Mathematical model

The cost-effectiveness analysis was conducted using an open dynamic model of HCV transmission and disease progression among current and former PWID, including diagnosis and treatment (see Figure 1; model equations in supporting information). The modelled population was stratified by

whether individuals were receiving opioid substitution therapy (OST) or not, which was used as a proxy for drug treatment centre attendance, where HepCATT took place.

People who start injecting drugs enter the model as susceptible individuals not on drug treatment. Individuals become HCV-infected at a rate dependent on the prevalence of infection, with those on OST/drug treatment having reduced risk of infection(24). Newly infected individuals either spontaneously clear their infection (antibody positive and RNA-negative) or become chronically infected (antibody and RNA-positive)(Figure 1b), which is life-long unless treated. Upon primary infection, liver disease progression occurs as in Figure 1c, with HCV-related death occurring from any stage after compensated cirrhosis. At any time, current injectors can initiate OST for an average duration and can die from drug related mortality or permanently cease injecting. Cessation from injecting is assumed to be independent of OST based on long-term cohort data of PWID from the UK that showed no clear association(25). Following cessation, individuals can no longer become HCV-infected, but can die due to natural causes and HCV (if infected) and can receive HCV treatment.

Chronically infected individuals can be diagnosed at a per capita rate depending on rates of testing and are either lost to follow up (LTFU) or engaged in the treatment pathway. Rates of testing depend on whether an individual is attending drug treatment or not. Engagement is defined as attending the hepatology clinic, whereupon they are treated at a per capita rate and either achieve effective cure (sustained virologic response, SVR) or fail treatment and continue to be chronically infected. Re-treatment of those who fail treatment occurs at the same rate as for initial treatment. Disease progression continues at a decreased rate in cured individuals who have compensated or decompensated cirrhosis and ceases in those with milder disease(26, 27). Cured individuals can be re-infected at the same rate as for primary infection, where upon disease progression continues from their current disease stage. Individuals who are LTFU are only re-engaged with the treatment pathway once they progress to compensated cirrhosis or more severe disease, or become in contact with HepCATT.

[insert figure 1]

Parameterisation and calibration of the standard-of-care model

The model was parameterised and calibrated to represent a generalised UK scenario using data from the annual unlinked anonymous monitoring (UAM) survey for PWID(28), baseline data collected for HepCATT(14), and HCV sentinel surveillance data collected from multiple testing settings(11). See Table 1. The UAM survey gave us the mean HCV antibody prevalence (52%) among PWID in England and Wales for 2015(28), or approximately 40% chronic prevalence(29). Estimates suggest 63% of PWID are currently on OST(28), with an average duration on OST of 8 months(30). We assume stable OST coverage and HCV prevalence among PWID in recent years(28, 31). Based on a recent Cochrane systematic review, we assume being on OST reduces the risk of HCV transmission by 59%(24). The percentage of chronically infected PWID who were diagnosed before the intervention was assumed to be 52%(28), with the standard-of-care testing rate at drug treatment centres (14% in last year) being estimated using baseline HepCATT data(14). The testing rate outside drug treatment centres was estimated through model calibration. The standard-of-care rate of engagement with the treatment pathway following diagnosis at drug treatment centres was estimated using baseline HepCATT data and a study on the cascade of care for different testing settings in England(11). The treatment rate for engaged individuals was estimated using baseline HepCATT data and was

assumed to be the same irrespective of where testing occurred. Although higher treatment rates may have been achieved recently, data is uncertain and so are only considered in the sensitivity analysis. We assumed the pre-2016 (pre-DAA) SVR was 49.5%(11) and the DAA SVR was 93%(32).

[insert table 1]

For the model calibration, 1000 parameter sets were sampled from the parameter distributions in Table 1. For each sampled parameter set, the transmission rate, OST recruitment rate and HCV testing rate for non-drug treatment settings were varied to fit the model (using MATLAB solver function lsqnonlin) to sampled values for the HCV chronic prevalence amongst current PWID in 2015, OST coverage and overall proportion diagnosed. This assumed the system was in steady state before 2016. Only parameter sets where the proportion diagnosed was within its uncertainty range were accepted as model fits; the model was always able to fit to the HCV prevalence and OST coverage. The resulting 720 model fits were used to simulate the standard-of-care and intervention scenarios. The calibration process is described further in the supporting information.

Standard-of-care comparator arm

The standard-of-care scenario assumes that testing, engagement and treatment are maintained at pre-HepCATT levels (Table 1) for individuals tested in all settings, with DAA therapy being undertaken in hospital clinics.

Intervention arm

Based on results of the HepCATT study, we modelled an intervention scenario where the odds of testing in drug treatment centres increased 2.5-fold and the odds of engagement onto the treatment pathway increased 10-fold from 2016(14). We also assumed that individuals attending drug treatment centres that were previously LTFU could be re-engaged onto the treatment pathway at the same rate as those newly diagnosed due to the nurse liaison intervention. Parameter ranges for the standard-of-care and intervention scenarios are given in Table 2.

[Insert Table 2]

Impact analysis

The number of infections and disease-related deaths averted between 2016 and 2030 or 2066 were estimated by comparing the projections of the standard-of-care and HepCATT model scenarios. The relative difference in the incidence and prevalence of HCV by 2030, and proportion of chronically infected PWID diagnosed was also estimated.

Costs and Utility Values

Costs and utilities from the literature are given in Table S7. Health utilities (quality adjusted life years [QALYs]) and HCV disease progression rates came from previous studies(26, 27, 33-35), with health utilities for HCV disease progression states(33) being multiplied by the baseline health utilities for PWID(36) or ex-PWID. Healthcare costs relating to HCV disease were taken from previous economic analyses(33, 35). Costs relating to the treatment pathway in hospitals using DAAs were based on the NHS treatment protocol (personal communication Graham Foster; see supplementary materials) and NHS reference costs(37). Costs were inflated to 2018 British Pounds using the Health and Community Hospital Service pay and prices index(38).

Costs for the HepCATT intervention (improving testing and engagement) were calculated from time allocation and resource use (number of antibody and RNA tests) data collected (top down approach) through interviews with nurses and keyworkers involved in the intervention from two cities. Staff time was allocated to either administration and management costs, diagnosis costs or engagement costs. Nurse salaries came from study records. Keyworker salaries and overhead costs (rent, utilities) were obtained from the drug treatment provider (Addaction) undertaking the intervention. Management, overheads and training costs were assigned to give a fixed yearly cost, with a greater cost in the first year due to additional staff training. Peer-workers were volunteers, so opportunity costs were applied equivalent to the minimum keyworker salary. Dried blood spot testing costs were obtained from the laboratory, which was a cost incurred by the intervention. Costs for testing per patient were calculated by summing staff and resource costs for the diagnosis stage and dividing by the number tested. The costs of engagement per patient were calculated by summing engagement costs (for all referred individuals regardless of attendance) and dividing by the number of patients engaged in the treatment pathway. For HepCATT, this included costs for getting individuals to hospital appointments, including keyworker and peer time, and for both arms included the costs of preliminary blood tests and fibroscan at the hospital. Costs for testing in other settings were taken from a published UK cost analysis of reflex testing(11), where samples are automatically tested for HCV RNA if they test antibody-positive. All testing was assumed to be reflex testing. Published costs for OST specialist prescribing were used, which incorporated staff time, prescribing costs and drug costs(38).

Cost-effectiveness analysis

Costs (2018 British Pounds, £1=$1.41) and health utilities were attached to each model state. The analysis used a 50-year time horizon to capture long-term effects of HCV infection and population prevention benefits of HCV treatment. The incremental cost-effectiveness ratio (ICER) was calculated as the difference in mean costs divided by the difference in mean QALYs between the intervention and the standard-of-care scenario. Cost-effectiveness was determined using the UK willingness-to-pay threshold of £20,000 per QALY gained(19).

Sensitivity analysis

A probabilistic sensitivity analysis (PSA) was performed for both modelled scenarios, and cost-effectiveness acceptability curves were plotted. The impact of parameter uncertainty on the incremental costs and QALYs was assessed using an ANCOVA analysis across the model fits(39).

Matched univariable sensitivity analyses examined the effect of:

a) varying the time horizon (100 or 15 years compared to 50 years) or discount rate (0% and 6% compared to 3.5%) across a wide range as recommended by NICE;

b) reducing the HCV drug cost by 80% (£7,796 per 12-week treatment course) to typify what the current cost of treatment in England could be, although the actual price is unknown;

c) increasing the treatment rate from engagement in all settings to 80% (from 16%-45%) within a year to determine how increased treatment uptake may affect the cost-effectiveness of the intervention; and

d) varying chronic HCV prevalence to 20% or 60% (compared to 40%) to capture the range of HCV prevalences observed in different UK or international settings(40, 41).

The impact of decreasing drug costs was also investigated in a threshold analysis, whereby the mean ICER was calculated for different drug costs to determine at what price the intervention becomes cost saving. Finally, an expected value of perfect information (EVPI) analysis was carried out(39) at the current full list DAA price.

Results

Impact analysis

The intervention is estimated to increase the number of PWID tested annually 2-fold (95%CrI 1.5-2.5) and the number treated 2.9-fold (95%CrI 2.3-6.1) (Figure S1). This increase in treatment is estimated to avert 75 deaths (95%CrI 37-129), 1330 infections (95%CrI 827-2040) and gain 1,607 QALYs over 50 years per 1000 PWID, or in England assuming 139,830 PWID(42) then it would avert 10,487 deaths (95%CrI 5,174-18,038), 185,974 infections (95%CrI 115,639-285,253) and gain 224,707 QALYs. This equates to 64% (95%CrI 50-72%) of all HCV-related deaths and 51% (95%CrI 30-67%) of all infections being averted over this period and a 56% (95%CrI 38-70%) decrease in chronic HCV prevalence and incidence by 2030 (Figure 2). The number of disease related deaths decreased by 29% (95%CrI 20-39%) over the same period.

[Insert Figure 2]

Costs of the intervention

There was one half-time nurse liaison associated with each setting during the intervention. Involvement of keyworker staff varied across settings with one keyworker supervising the peer workers for between 1 or 2 days a week. The remaining keyworkers at the two settings each had 1-1.5 days of training for HepCATT. In one setting, there were 9 keyworkers who each spent 0.03 full-time equivalent (FTE) or 0.28 FTE altogether on HepCATT and 6 peers who spent 0.14 FTE altogether. In the second setting, there were 48 keyworkers and 15 peers totalling 0.38 FTE and 0.5 FTE, respectively. Table 3 shows the allocation of HepCATT costs to different stages of the diagnosis and engagement pathway; Table S8 gives a breakdown of standard-of-care costs. Once set-up, the ongoing yearly fixed costs of HepCATT are £12,385 (includes one round of peer worker training), while the average cost to engage a previously undiagnosed or diagnosed patient on to treatment is £682 and £600, respectively. All stages of the pathway to engagement are more costly than the standard-of-care reflecting the increased staff time associated with HepCATT.

[Insert Table 3]

The breakdown of costs applied over the 50-year time horizon per 1000 PWID are shown in Table 4. The total incremental cost of the intervention was £12.8 million for the full list drug price. This was made up of extra expenditure (£15.8 million), mainly in testing and engagement (HepCATT, £1.0 million) and HCV treatment (PWID and ex-injectors, £14.8 million), and cost savings (£3.0 million) in HCV-related healthcare costs. For the England population of PWID, the incremental costs increase to £1,789.8 million for the full price of DAAs, with the intervention costing £144.8 million over 50-years or £8.8 million to 2030 (discounted). The annual intervention cost is more than the standard-of-care scenario until 2048 (Figure S2).

[Insert Table 4]

Base case cost-effectiveness analysis

Table 5 shows the results of the cost-effectiveness analysis over 50-years. For the full list DAA price, the Intervention costs £12.8 million more than the standard-of-care scenario, but accrues 1,607 extra QALYs, giving a mean ICER of £7,986 per QALY gained. The cost-effectiveness plane (Figure S3) shows that all simulations are below the £20,000 per QALY willingness-to-pay threshold.

[Insert Table 5]

Sensitivity analysis

The results were robust to numerous univariable sensitivity analyses, with the ICER remaining below the £20,000 per QALY willingness-to-pay threshold (Figure 3). Decreasing the discount rate, lengthening the time horizon or reducing the HCV treatment drug cost by 80% all decreases the mean ICER making the intervention more cost-effective. Indeed, an 80% decrease in drug cost causes the total incremental cost of the intervention to reduce to £1,145,245 per 1000 PWID or £160,139,908 for an England population of 139,830 PWID. Similarly, increasing the proportion of engaged individuals that start treatment to 80% (from 16%-45%) decreases the ICER to £4,321 per QALY gained, and achieves a 77% (95%CrI 57-87%) reduction in incidence by 2030. Assuming a lower chronic HCV prevalence (20%) does not affect the ICER much (£5,692 per QALY), while assuming higher chronic prevalence (60%) increases the ICER to £17,797 per QALY.

[Insert Figure 3]

The threshold analysis (figure S4) shows the intervention becomes cost-saving (costs less than the standard-of-care comparator and saves more QALYs) for a 90% reduction in drug price (£3,898 per 12-week regimen). The ANCOVA (figure S5) shows that uncertainty in the annual HCV-related healthcare costs accounted for 80% of the variation in incremental costs, while uncertainty in the treatment rate and utility values for mild disease (F0-F1) resulted in 59% of the variability in incremental QALYs. The EVPI was zero as all simulations are cost-effective at the £20,000 per QALY willingness-to-pay threshold.

Discussion

Introducing a nurse led intervention (with peer support) to improve the HCV testing and engagement to care of PWID attending drug treatment centres is cost-effective (£7,986 per QALY saved) at current list prices for DAA HCV treatment (£39,000 per treatment), and becomes cost-saving if drug costs decrease to £3,900 per treatment. Moreover, if the intervention were scaled up

to all drug treatment centres in England, it could avert 51% of infections and 64% of HCV-related deaths over a 50-year period and reduce incidence by 56% by 2030. Optimising the intervention further, with 80% of people being treated within a year of engagement results in the intervention becoming more cost-effective (£4,321 per QALY for full list price of DAAs) and could reduce incidence by 77% by 2030. Because most on-going HCV transmission in the UK is among PWID(2), these impact projections suggest that this intervention could be an important component of the NHS-England initiative to reach the WHO elimination targets of decreasing HCV incidence by 90% by 2030 or earlier. National estimates for scaling up the intervention suggest it would cost £144.8 million over the next 50 years or £8.8 million by 2030 (discounted).

Strengths and Limitations

The main strength of our study is that we evaluate a real-life intervention using empirical data on the outcomes of the intervention and costs. We also use a dynamic HCV transmission model to capture the prevention benefits of the intervention, while incorporating uncertainty in all model parameters. Nonetheless, potential limitations still exist.

Firstly, the estimates for fixed intervention costs, which include management (staff time and building costs) and training costs, are based on two of the three study settings. This was deemed appropriate because these two settings were of differing sizes in terms of PWID population but still had similar set up costs.

Secondly, a generic English setting was modelled to make our results relevant to the whole of England. However, OST coverage and HCV prevalence vary across England and the intervention's cost-effectiveness may depend on these inputs. Indeed, the cost-effectiveness of the intervention diminishes at higher chronic HCV prevalences (60%) due to greater reinfection(43), although it is still cost-effective. In contrast, variation in the coverage of OST (proportion of PWID currently on OST) is unlikely to affect the cost-effectiveness of the intervention, with the uncertainty included in our analysis (60-65%) not effecting our results. However, the impact of the intervention will be lessened at lower OST coverage levels because the reach of the case-finding strategy will be reduced. This could also occur if many PWID inject stimulants which OST is not an effective intervention for.

Lastly, the analysis used data on the overall proportion of PWID diagnosed with HCV to obtain a testing rate in settings other than drug treatment centres. Although a wide range of testing rates were used (0.01-0.45 per year) in the standard-of-care comparator, it is likely that testing rates have increased across all services because of the on-going expansion of HCV treatment. It is unclear how this will affect the cost-effectiveness of this intervention, although solely improving the proportion of engaged individuals that start treatment improves the cost-effectiveness of the intervention in our sensitivity analyses.

Comparison with other studies

This is the first UK and European study to evaluate the cost-effectiveness of a real-life case-finding intervention among PWID since the emergence of DAA therapies. Our findings are consistent with other studies which find case-finding among PWID to be cost-effective when sufficient diagnosed individuals are treated(9, 12, 13, 44), with some of these interventions also providing onsite HCV treatment in drug treatment centres to improve linkage to treatment(45). Only two of these studies considered the use of new DAA therapies(12, 44), finding that HCV screening through drug

treatment centres with active linkage to treatment was cost-effective in New York city (<$35,000 per QALY gained). Two other European studies before the emergence of DAA therapies considered the cost-effectiveness of case-finding interventions for PWID, with both including scenarios that assumed the use of a 'DAA-like' treatment with higher drug cost and SVR. One UK study found introducing dried blood spot testing in drug treatment centres was cost-effective at less than £15,000 per QALY when assuming the use of interferon-based treatments or first generation DAAs(9). Another study from the Netherlands evaluated testing in drug treatment centres (comparator was no testing), finding it to be similarly cost-effective (Euro 9,056 per QALY) to our intervention (at full list price). However, they assumed 77% of diagnosed cases were referred and 37% of these cases were treated (13), considerably higher than we assumed for our analysis.

Conclusions and implications

Drug treatment centres are a high yield setting for identifying individuals that require HCV treatment(11). Our study provides evidence that introducing HCV nurse facilitators in drug treatment centres is highly cost-effective, potentially cost-saving if HCV drug prices fall sufficiently, and if scaled-up could reduce HCV incidence by 56% by 2030 for an estimated direct intervention cost of £8.8 million if scaled up nationally. This could contribute considerably to national targets for achieving HCV elimination as a public health problem. Better engagement and so greater impact could be achieved if this intervention also provides HCV treatment onsite as has been piloted in other settings(15).

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Tables

Table 1 Demographic and epidemic model parameters.

Parameter Description	Point Estimate	Sampled Distribution	Rationale	Source
Rate of cessation of injecting per year – set as 1/ injecting duration	1/11.5	Injecting duration Uniform (8,15)	Mean injecting duration 11.5 years, assumption for sampled range	(45)
Drug related death rate per year	0.0073	Poisson Distribution mean=0.73 /100	Data suggests 45-84 deaths per 10,000 person years among opiate users identified from drug treatment and criminal justice records in England (2005-2009)	(46)
Death rate amongst individuals that have ceased injecting (per year)	0.026	Life expectancy Uniform (70,80) Age at initiation of injecting Uniform (20,30)	1/(life expectancy-age at initiation of injecting-injecting duration)	World bank life expectancy data, UAM data
Initiation rate of new injectors (injectors per year)	Estimated through model calibration		Fitted assuming a constant population size of 1000 or UK population size and sampled death and cessation rates for current injectors	
Proportion of treated individuals that achieve SVR pre 2016	0.49	Uniform (0.483,0.507)	UK SVR data from sentinel surveillance	(11)
Proportion of treated individuals that achieve SVR post 2016	0.93	Uniform (0.88,0.98)	Results from SIMPLIFY phase 4 trial using sofosbuvir and velpatisvir in people with recent injection drug use	(32)
Rate at which people start attending drug treatment centres (per year)	Estimated through model calibration		Fitted to give a coverage of OST (proportion of PWID currently on OST) that is uniformly sampled between 60-65% from Unlinked Anonymous Monitoring Survey	(40)
Rate at which people stop attending drug treatment centres (per year)	1/(years on OST)	Years on OST Uniform (0.33,1)	Duration on OST was 8 months (4-12 months) in cohort of PWID in UK	(30)
Reduced risk of HCV transmission due to being on OST	0.41	Lognormal (0.22,0.74)	Cochrane Review	(24)

Parameter Description	Point Estimate	Sampled Distribution	Rationale	Source
HCV Ab prevalence	52%	Normal (CI 51-55%)	From literature	(28)
Baseline transmission rate	Estimated through model calibration		Fitted using sampled Ab prevalence * (1-proportion of infections that spontaneously clear).	
Proportion of infections that spontaneously clear	0.26	Uniform (0.22,0.29)	From literature	(29)
Rate at which individuals complete treatment = 1/treatment duration (per year)	52/12	Constant	12 weeks for DAA treatment	NICE guidelines

UAM – Unlinked Anonymous Monitoring survey; NICE – National Institute for Clinical Excellence; OST – opioid substitution therapy

Table 2: Parameters related to HCV treatment pathway for the standard-of-care and intervention scenario

Parameter	**Standard-of-care**	**Source**	**Intervention**	Source
Testing Rate per year				
Drug Treatment Centres	0.140 (0.075-0.259)	HepCATT baseline data(47)	0.332(0.167-0.586)	HepCATT intervention dat; see supplementary information for more details (47)
Other Settings and Ex-injectors	Varied to give required proportion of injectors diagnosed (mean 52%) Posterior median 0.035 (0.001-0.450)		Same as for standard-of-care	Assume intervention has no impact on other settings
Engagement Rate per year				
From Drug Treatment Centres within 1 year of diagnosis	0.092 (0.035-0.242)	HepCATT baseline data(47)	0.741 (0.206-1.634)	HepCATT intervention data(47)
From Other Diagnosis settings within 1 year of diagnosis	0.092 (0.035-0.242)	HepCATT baseline data(47)	Same as for standard-of-care	
From Drug Treatment Centres after 1 year since diagnosis	0 unless disease stage is F4 or above	Assumption that after 1 year patients are lost to follow up until symptomatic	0.741 (0.206-1.634)	HepCATT intervention data(47)
From Other Settings after 1 year since diagnosis	0 unless disease stage is F4 or above	Assumption that after 1 year patients are lost to follow up until symptomatic	Same as standard-of-care	Assume intervention has no impact on other settings
Treatment rate per year				
All Settings	0.330 (0.170-0.590)	HepCATT baseline data(47)	Same as for standard-of-care	Assume intervention has no impact on treatment at hospital clinic
Proportion of treated individuals that achieve SVR post 2016	0.93	Uniform (0.88,0.98)	Results from SIMPLIFY phase 4 trial using sofosbuvir and velpatisvir in people with recent injection drug use	(32)

Table 3: Costs related to testing and linkage to treatment

Step		Standard-of-care Cost	Intervention Cost	Source
HepCATT startup cost for first year including management staff time during project initiation, nurse staff training and peer worker training		0	[£25,403-£34,712]	HepCATT costing analysis (see supplementary information)
Second and Subsequent Years fixed costs for HepCATT includes management, staff project oversight and one round of peer worker training		0	[£10,951-£13,818]	
Costs per Test (includes staff time and test costs)	Ab negative	£53 +/- 10%	[£106 - £161]	(11) and HepCATT costing analysis (see supplementary information)
	Ab positive	£119 +/- 10%	[£150 - £212]	
	Previous known SVR (Ab+)	£119 +/- 10%	[£146 - £207]	
Costs per Engagement (includes staff referral costs and preliminary blood tests and fibroscan at the hospital)	From Diagnosed	£409 +/- 10%	[£124-£212] (referral cost) +[£332±10%] (at hospital)	Standard-of-care referral costs from (11), hospital costs from expert opinion (correspondence Graham Foster) Intervention referral costs from HepCATT costing analysis (see supplementary information)
	From Lost to Follow Up	£409 +/- 10% (later stages of disease progression only)	[£96-£124] (identifying patient) +[£124-£212] (referral cost) +[£332±10%] (at hospital)	
Cost per Treatment	Treatment Monitoring	£394 +/- 10%		Expert opinion (correspondence Graham Foster and supplementary information for details)
	Weekly Drug Cost	£3,249 +/-10%		Assume full current list price (48)

Costs sampled from uniform distributions. Assumes population size of 1000 people who inject drugs.

Table 4: Breakdown of discounted costs over 50-year time horizon

	Standard-of-care mean	Intervention mean	Difference
HCV related Healthcare	£9,306,667	£6,261,626	-£3,045,041
HCV treatment ex-PWID	£3,318,512	£5,001,366	£1,682,854
HCV treatment PWID	£1,894,516	£14,998,725	£13,104,208
Testing and Engagement *	£424,988	£1,460,213	£1,035,225
OST	£48,078,808	£48,137,935	£59,127
Total	£63,023,491	£75,859,865	£12,836,374

*Includes cost of testing and engagement in drug treatment centres and other settings and testing and engagement of ex-injectors. Initial population size of PWID is 1000, injector population is maintained at 1000, with people ceasing injecting also followed for the 50-year time horizon.

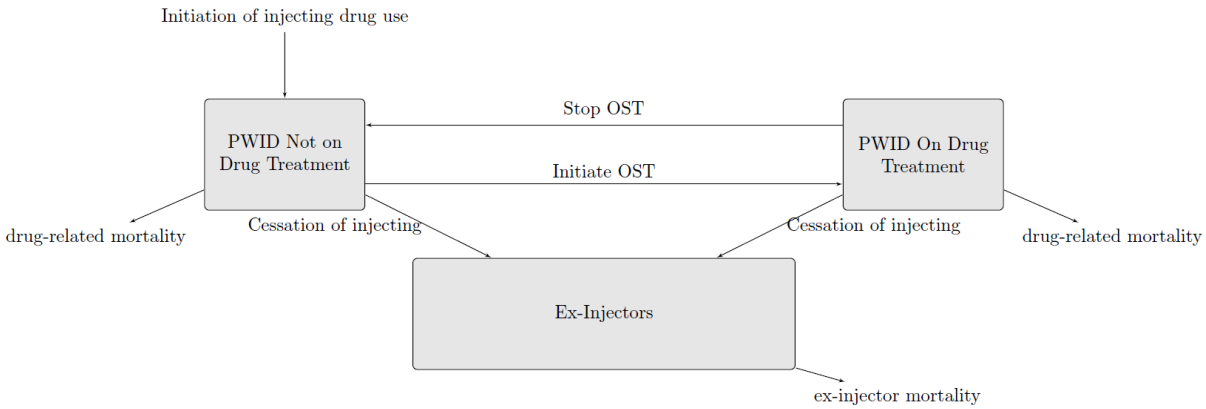
Table 5: Cost-effectiveness results (Initial population size 1000 current injectors)

	Mean Total Costs	Incremental Costs	Mean Total QALYs	Incremental QALYs	mean ICER (£ per QALY)
Standard-of-care	£63,023,491		36,865		
Intervention	£75,859,865	£12,836,374	38,472	1,607	£7,986

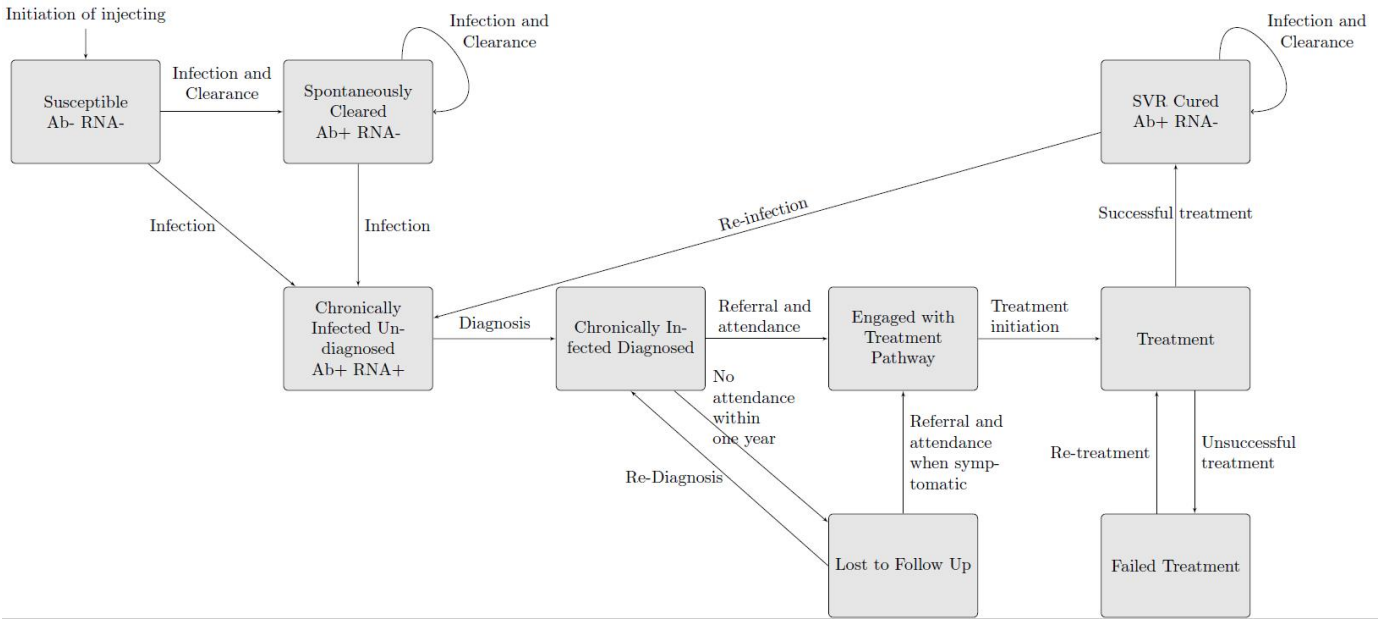
Figures

Figure 1: Schematic of the model structure for (a) population stratification by PWID and harm reduction status (b) infection, diagnosis and treatment, and (c) disease progression.

a)



b)



c)

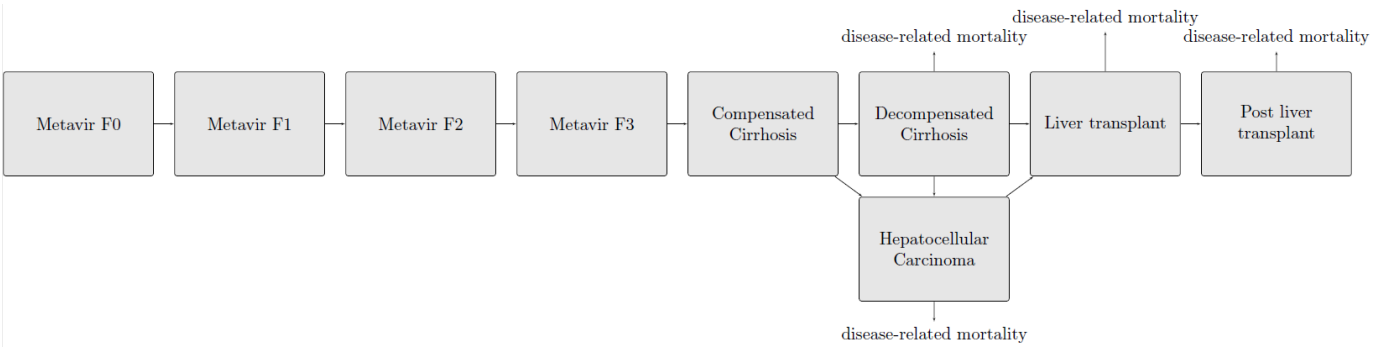
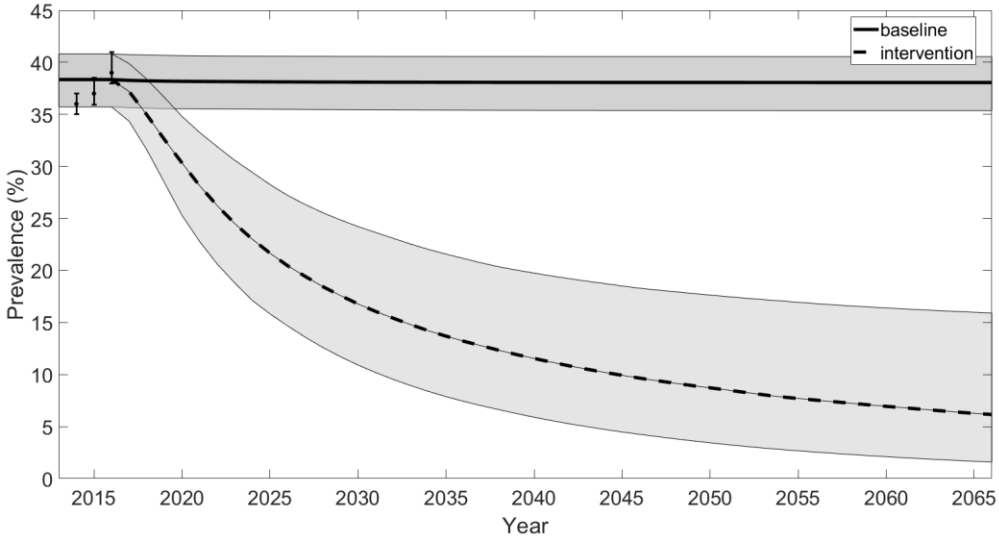


Figure 2: Model projections of the (a) chronic prevalence and (b) incidence of HCV with and without the HepCATT intervention, with data on the prevalence of HCV in 2016 (which the model was fit too) and incidence of HCV for 2015 and 2016 (which the model was not fit too) being shown for comparison. Points are the mean of the data estimates with the whiskers showing the 95% confidence intervals. The black solid or dashed lines show the median of the model projections with the shaded areas denoting the 95% central range of the model projections.

(a) Chronic prevalence of HCV



(b) Incidence of HCV

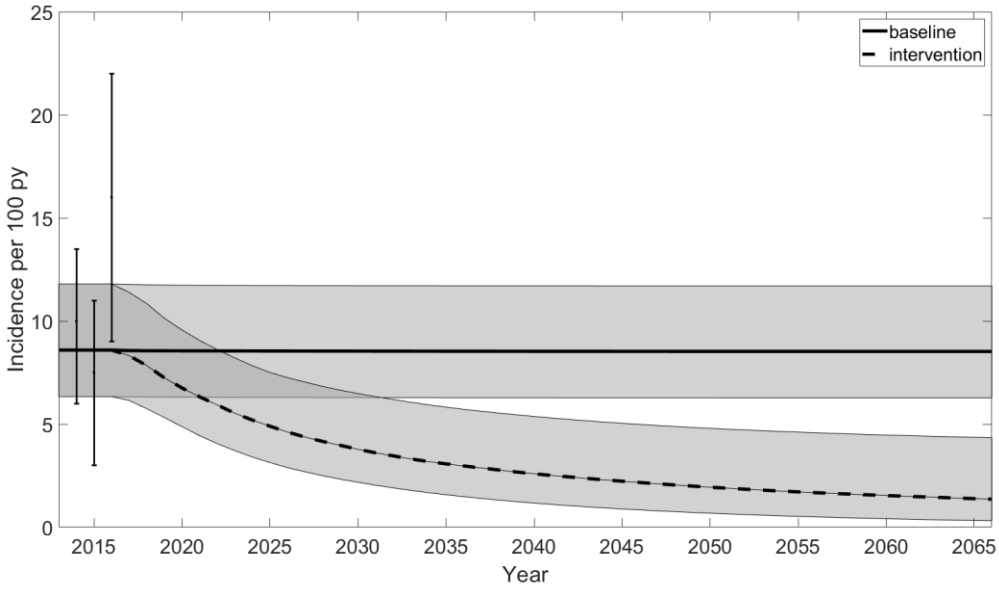
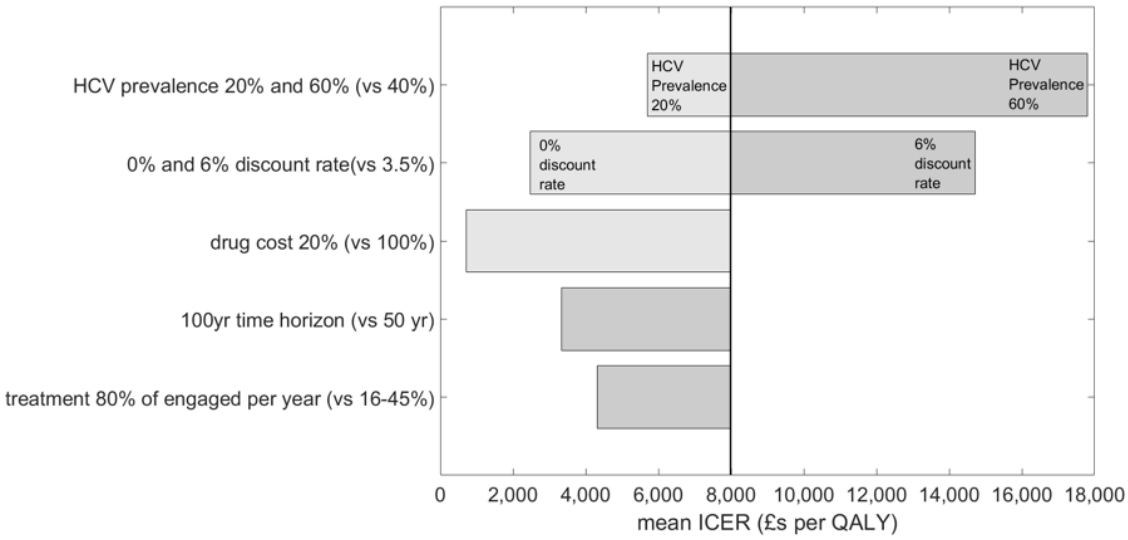


Figure 3: Tornado plot showing the effect of changing different model assumptions on the mean ICER with increased parameters in the darker shade of grey.



Supporting Information

Model Equations

A. Infection and treatment sub-model

This sub-model stands alone and can be used to investigate the impact of treatment on the prevalence of HCV a population of people who inject drugs.

Notes: The letter $S_i^{k,m}$ denotes a susceptible individual. The superscript k is either 0 or 1 denotes injector and ex-injector respectively. The superscript m is from 1,2,..9 denoting the disease progression state (more on this sub-model below). The subscript i is either 0 or 1 and denotes off or on OST respectively.

Table S1: Definition of the model state variables

Variable	Symbols
Susceptible individuals	$S_i^{k,m}$
Exposed individuals but not infected (Ab+, RNA-)	$E_i^{k,m}$
Chronically infected individuals (Ab+, RNA+)	$C_i^{k,m}$
Diagnosed infected individuals	$D_i^{k,m}$
Infected individuals engaged in treatment pathway	$N_i^{k,m}$
Lost to follow up infected individuals	$L_i^{k,m}$
Infected individuals undergoing Treatment	$T_i^{k,m}$
Individuals who have attained SVR and are no longer infected	$V_i^{k,m}$
Infected individuals who have Failed treatment	$F_i^{k,m}$

Table S2: Definition of the model parameters

Parameters	Symbols	Units
Infection rate	λ	per year
Relative risk of transmission/acquisition of HCV when on OST	B	None
Proportion of infections that spontaneously clear	δ	None
Testing rate	τ_i	Per year
Engagement rate from diagnosed	ρ_d	Per year
Engagement rate from lost to follow up	ρ_L^m	Per year
Transition rate from diagnosed to lost to follow up	ϵ	Per year

Parameters	Symbols	Units
Treatment rate from engaged	ω^m	Per year
Length of time on treatment	σ	Years
Proportion of treatments that attain SVR	α	None
Death rate in injectors	μ_1	Per year
Death rate in ex-injectors	μ_5	Per year
Inflow of new injectors	θ	People per year

Notes: The testing rate depends on contact with drug treatment services (OST). We assume that those on OST ($i = 1$) have an increased rate of testing. The engagement rate from Lost to follow up (ρ_L) depends on the current disease progression state. At baseline, we assume that $\rho_L = 0$ for $m = 1,2,3$ amd $\rho_L = \rho_d$ for $m > 3$. The treatment rate from engaged also depends on the current disease progression state. For $m < 7$ the treatment rate is non-zero, otherwise it is zero.

Force of infection

Define:

$$I_i^{0,m} = \sum C_i^{0,m} + D_i^{0,m} + L_i^{0,m} + N_i^{0,m} + F_i^{0,m}$$

which gathers together all of the infectious individuals in the population within the same OST status

Define:

$$P_i^{0,m} = \sum S_i^{0,m} + E_i^{0,m} + C_i^{0,m} + D_i^{0,m} + L_i^{0,m} + N_i^{0,m} + T_i^{0,m} + V_i^{0,m} + F_i^{0,m}$$

Which gathers together all individuals in the population within the same OST status.

The base force of infection is given by

$$\phi = \frac{\lambda \sum_{m=1}^{m=9} \mathrm{I}_0^{0,\mathrm{m}} + \mathrm{B} I_1^{0,m}}{\sum_{m=1}^{m=9} \mathrm{P}_0^{0,\mathrm{m}} + \mathrm{B} P_1^{0,m}}$$

Define Λ_i as the multiplier of the force of infection which depends on OST status where

$$\Lambda_0 = 1, \Lambda_1 = \mathrm{B},$$

This allows the following system of equations for the infection part of the model

$$\dot{S}_i^{0,m} = \theta - (\mu_1 + \nu + \Lambda_\mathrm{i}\phi) S_i^{0,m}$$

$$\dot{E}_i^{0,m} = \delta\Lambda_i\phi S_i^{0,m} - (\mu_1 + \nu + (1-\delta)\Lambda_i\phi)E_i^{0,m}$$
$$\dot{C}_i^{0,m} = (1-\delta)\Lambda_i\phi S_i^{0,m} + (1-\delta)\Lambda_i\phi E_i^{0,m} + (1-\delta)\Lambda_i\phi V_i^{0,m} - (\mu_1 + \nu + \tau_i)\, C_i^{0,m}$$
$$\dot{D}_i^{0,m} = \tau_i C_i^{0,m} - (\mu_1 + \nu + \epsilon + \rho_d)D_i^{0,m}$$
$$\dot{L}_i^{0,m} = \eta D_i^{0,m} - (\mu_1 + \nu + \rho_l^m)L_i^{0,m}$$
$$\dot{N}_i^{0,m} = \rho_d D_i^{0,m} + \rho_L^m L_i^{0,m} - (\mu_1 + \nu + \omega^m)N_i^{0,m}$$
$$\dot{T}_i^{0,m} = \omega^m N_i^{0,m} - (\mu_1 + \nu + \sigma^{-1})T_i^{0,m}$$
$$\dot{V}_i^{0,m} = \alpha\sigma^{-1}T_i^{0,m} - (\mu_1 + \nu + (1-\delta)\Lambda_i^{0,\mathrm{m}}\phi)V_i^{0,m}$$
$$\dot{F}_i^{0,m} = (1-\alpha)\sigma^{-1}T_i^{0,m} - (\mu_1 + \nu + \omega^m)F_i^{0,m}$$

When ex-injectors are included in the model ($k = 1$), there are no new infections in ex-injectors, but they can be diagnosed and treated as for current injectors.

B. Demographics sub-model

Table S3: Definition of the model state variables

Variable	Symbols Example
Susceptible injector, not on OST	$S_0^{0,m}$
Susceptible injector, on OST	$S_1^{0,m}$
Susceptible ex-injector (not on OST)	$S_0^{1,m}$

Table S4: Definition of the model parameters

Parameter	Symbol	Units
Transition rate from off OST to on OST	β	Per year
Transition rate from on OST to off OST	γ	Per year
Injecting cessation rate	ν	Per year

The terms for the differential equations for this part of the model are given by the following system ($\underline{OS}$), where $OS_i^{k,m}$ are the terms concerning movement between OST and injecting states for variable $S_i^{k,m}$ and are valid for all infection sub-model states (different variable letters) and disease progression states (superscript m)

$$\underline{OS} = \begin{pmatrix} OS_0^{0,m} \\ OS_1^{0,m} \\ OS_0^{1,m} \end{pmatrix} = B\underline{S}$$

$$\underline{S} = \begin{pmatrix} S_0^{0,m} \\ S_1^{0,m} \\ S_0^{1,m} \end{pmatrix},$$

$$B = \begin{pmatrix} -\beta - \nu & \gamma & 0 \\ \beta & -\gamma - \nu & 0 \\ \nu & \nu & 0 \end{pmatrix}$$

C. Disease Progression sub-model

The following sub-model variables and terms can be included to explore disease progression in the population.

Table S5: Definition of the model state variables

State	Symbol Example
Metavir F0	$C_i^{0,1}$
Metavir F1	$C_i^{0,2}$
Metavir F2	$C_i^{0,3}$
Metavir F3	$C_i^{0,4}$
Metavir F4 (compensated cirrhosis)	$C_i^{0,5}$
Decompensated cirrhosis	$C_i^{0,6}$
Hepatocellular Carcinoma	$C_i^{0,7}$
Liver Transplant	$C_i^{0,8}$
Post Liver Transplant	$C_i^{0,9}$

Table S6: Definition of the model parameters

Parameter	Symbol
Yearly progression rate from f0 to f1	ζ_1
Yearly progression rate from f1 to f2	ζ_2
Yearly progression rate from f2 to f3	ζ_3
Yearly progression rate from f3 to compensated cirrhosis	ζ_4
Yearly progression rate from compensated cirrhosis to decompensated cirrhosis	ζ_5
Yearly progression rate from compensated cirrhosis or decompensated cirrhosis to hepatocellular carcinoma	ζ_6

Parameter	Symbol
Yearly progression rate from decompensated cirrhosis or HCC to liver transplant	ζ_7
Yearly progression rate from liver transplant to post liver transplant	ζ_8
Decompensated cirrhosis related death rate per year	ζ_6
Hepatocellular carcinoma related death rate per year	d_7
Liver transplant related death rate per year	d_8
Post liver transplant related death rate per year	d_9
Relative risk for progression rate from compensated to decompensated cirrhosis following SVR	e_5
Relative risk for progression rate from compensated cirrhosis to HCC following SVR	e_6

These terms in the equations are concerned with movement through the disease states. Infection and treatment are described separately above. $DY_i^{k,m}$ denotes the terms in the ordinary differential equation of disease category m for susceptible individuals who have previously been treated and $DC_i^{k,m}$ for infected individuals. These terms can be found in the equations for all values of i, j, k and m.

$$\begin{pmatrix} DC_i^{k,1} \\ DC_i^{k,2} \\ DC_i^{k,3} \\ DC_i^{k,4} \\ DC_i^{k,5} \\ DC_i^{k,6} \\ DC_i^{k,7} \\ DC_i^{k,8} \\ DC_i^{k,9} \end{pmatrix}$$

$$= \begin{pmatrix} -\zeta_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \zeta_1 & -\zeta_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \zeta_2 & -\zeta_3 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \zeta_3 & -\zeta_4 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \zeta_4 & -\zeta_5 - \zeta_6 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \zeta_5 & -\zeta_6 - \zeta_7 - d_6 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \zeta_6 & \zeta_6 & -\zeta_7 - d_7 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \zeta_7 & \zeta_7 & -\zeta_8 - d_8 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \zeta_8 & -d_9 \end{pmatrix} \begin{pmatrix} C_i^{k,1} \\ C_i^{k,2} \\ C_i^{k,3} \\ C_i^{k,4} \\ C_i^{k,5} \\ C_i^{k,6} \\ C_i^{k,7} \\ C_i^{k,8} \\ C_i^{k,9} \end{pmatrix}$$

$$\begin{pmatrix} DY_i^{k,1} \\ DY_i^{k,2} \\ DY_i^{k,3} \\ DY_i^{k,4} \\ DY_i^{k,5} \\ DY_i^{k,6} \\ DY_i^{k,7} \\ DY_i^{k,8} \\ DY_i^{k,9} \end{pmatrix}$$

$$= \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -e_5\zeta_5 - e_6\zeta_6 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & e_5\zeta_5 & -\zeta_6 - \zeta_7 - d_6 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & e_6\zeta_6 & \zeta_6 & -\zeta_7 - d_7 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \zeta_7 & \zeta_7 & -\zeta_8 - d_8 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \zeta_8 & -d_9 \end{pmatrix} \begin{pmatrix} V_i^{k,1} \\ V_i^{k,2} \\ V_i^{k,3} \\ V_i^{k,4} \\ V_i^{k,5} \\ V_i^{k,6} \\ V_i^{k,7} \\ V_i^{k,8} \\ V_i^{k,9} \end{pmatrix}$$

As an example as to how this all works together, below are two differential equations for susceptible and chronically infected individuals who are current injectors ($k = 0$), on OST ($i = 1$) and in Metavir state F0 ($m = 1$).

$$\dot{S}_1^{0,1} = -\left(\mu_1 + \nu + \Lambda_{1,1}\phi\right)S_1^{0,1} + \beta S_0^{0,1} - \gamma S_1^{0,1}$$
$$\dot{C}_1^{0,1} = -(\mu_1 + \nu + \gamma)C_1^{0,1} + \beta C_0^{0,1} + (1-\delta)\Lambda_1\phi S_1^{0,1} - \zeta_1 C_1^{0,1}$$

Model Calibration procedure

The sampled HCV prevalence and proportion of PWID diagnosed was used to fit the overall infection rate and HCV testing rate in other settings (using pre-DAA treatment efficacy). Fitting was carried out using the least squares non-linear fitting function, lsqnonlin, in Matlab in a sub-model without disease progression that does not include ex-injectors. Using the testing rate and infection rate found using this method the initial conditions of the full model with disease progression are obtained by running the system to steady state.

Table S7 Costs and Utility parameter values

Annual Costs	**Mean Value 2018 £**	**Distribution**	**Source**
OST specialist prescribing in community including staff time	2,901 xPPI	-	(38)
HCV Uninfected	0	-	(33)
F0 and F1 Mild HCV	188	Gamma (0.659,289)xPPI	
F0 and F1 Mild HCV SVR	390	Gamma (28.81,8.98)xPPI	
F2 and F3 Moderate HCV	1,031	Gamma (0.485,2038)xPPI	
F2 and F3 Moderate HCV SVR	390	Gamma (88.85,8.07)xPPI	
Compensated Cirrhosis	1,574	Gamma (0.211,7452)xPPI	
Compensated Cirrhosis SVR	1,574	Gamma (24.23,46.95)xPPI	
Decompensated cirrhosis	12,930	Gamma (0.901,13974)xPPI	
Hepatocellular Carcinoma	12,053	Gamma (0.926,12251)xPPI	
Liver transplant	40,818	Gamma (89.75,304.5)xPPI	(35)
Hospital costs year of transplant	13,974	Gamma (13.78,686.4)xPPI	
Post-transplant	2,059	Gamma (15.22,91.1)xPPI	
Health Utility Weights			
Uninfected			

Ex / non-PWID	0.85	Uniform (0.8-0.9)	assumption
PWID	0.73	Uniform (0.68-0.78)	(36)
Mild HCV (F0 and F1)			
Without Treatment	0.77	Beta (521.2375,155.6943)	(33)
SVR	0.82	Beta (65.8678,14.4588)	
Moderate HCV (F2 and F3)			
Without Treatment	0.66	Beta (168.2461, 86.6723)	
SVR	0.72	Beta (58.0608,22.592)	
Compensated Cirrhosis			
Without Treatment	0.55	Beta (47.1021, 38.5381)	
SVR	0.61	Beta (58.0608,37.1124)	
Decompensated cirrhosis	0.45	Beta (123.75, 151.25)	
Hepatocellular Carcinoma	0.45	Beta (123.75, 151.25)	
Liver transplant	0.45	Beta (123.75, 151.25)	
Post-transplant	0.67	Beta (59.2548, 29.1852)	

PPI payment price index (38)

Table S8: Disease Progression rates

Parameter	**Distribution**	**Source**
Yearly progression rate from F0 to F1	0.0529-0.2095	PWID specific instantaneous rates from (34) – sampled from normal distribution
Yearly progression rate from F1 to F2	0.0216-0.1013	
Yearly progression rate from F2 to F3	0.0450-0.1145	
Yearly progression rate from F3 to compensated cirrhosis	0.0513-0.1838	
Yearly progression rate from compensated cirrhosis to decompensated cirrhosis	0.0166-0.0921	Instantaneous rates calculated from sampled beta distributions of transition probabilities in (35)
Yearly progression rate from compensated cirrhosis or decompensated cirrhosis to hepatocellular carcinoma	0.0003-0.0684	
Yearly progression rate from decompensated cirrhosis or HCC to liver transplant	0.0062-0.0962	
Yearly progression rate from liver transplant to post liver transplant	1.0423-2.4412	
Decompensated cirrhosis related death rate per year	0.1063-0.1842	
Hepatocellular carcinoma related death rate per year	0.3904-0.7697	

Parameter	Distribution	Source
Liver transplant related death rate per year	0.0911-0.4348	
Post liver transplant related death rate per year	0.0280-0.1016	
Relative risk for progression rate from compensated to decompensated cirrhosis (ρ_5) following SVR	0.07 (95%CI 0.03,0.2)	Sampled from transformed lognormal distribution (26)
Relative risk for progression rate from compensated cirrhosis to HCC (ρ_6) following SVR	0.23 (95%CI 0.16,0.35)	Sampled from transformed lognormal distribution (27)

Costings Analysis

What was included?

Staff time, buildings use, capital equipment, training costs, supplies, consultancy.

How was it measured?

- Staff type and time was determined by questioning a subset of the staff involved. Nurse facilitators were interviewed as well as the keyworkers involved in the buddy system operation in both Lincoln and Liverpool.
- Buildings use was determined using fire safety floorplans of the buildings and questioning staff on room use to obtain an allocation percentage of the rent (and maintenance) per year.
- Capital equipment was only laptops.
- For supplies the cost of the testing kits and surgical gloves was included.
- Training costs included staff time for training as well as the cost of providing the training itself where known. In one of the settings, the nurse facilitator underwent lots of training at the start of the intervention but only the staff time was included in the costing as we did not have costs of the courses attended.
- Consultancy was Hepatitis C Trust training that was given. Expenses from the Hepatitis C Trust were included as well as their usual course fee (which was not paid in this instance) to obtain a full economic cost rather than the financial cost.
- Expenses for meetings and training events were recorded although only those incurred for non-research purposes were included in the unit costs of the intervention

Where are the reference costs from?

Staff salaries for keyworkers were obtained from Addaction (mid value of the range given was used). Nurse facilitator salaries were obtained from the HepCATT study budgets. NHS consultant salaries for hepatologists were taken from the NHS website. Volunteers (both peers and buddies) were assumed to have an opportunity cost of the lowest paid key worker (one of the peers became a peer worker after the study). Dried blood spot test costs (undertaken by Alere), were obtained from HepCATT study records. Buildings and maintenance costs were obtained from Addaction (including rent, utilities, and cleaning).

What assumptions were made?

Costs were separated out into fixed costs, which don't depend on the number of tests or patients seen, and variable costs. A fixed yearly cost was calculated for running the intervention using the management and training costs. Management costs included line management of staff, meetings for ongoing management of the intervention and training costs included staff training specific to the intervention. It was assumed that in the first year (start up) of the intervention all of the costs would apply and in subsequent years there would be one training session by the Hep C Trust, costing £2500 on average.

For diagnosis costs, personnel time per test was calculated using the outcome data for each site, then the cost per test depended on whether the person tested was uninfected (antibody negative), in which case there was only the cost of the Ab test and a pair of gloves. Otherwise, the laboratory cost of the RNA test was added. For individuals who have been previously treated, only the RNA test cost was assumed in addition to personnel time.

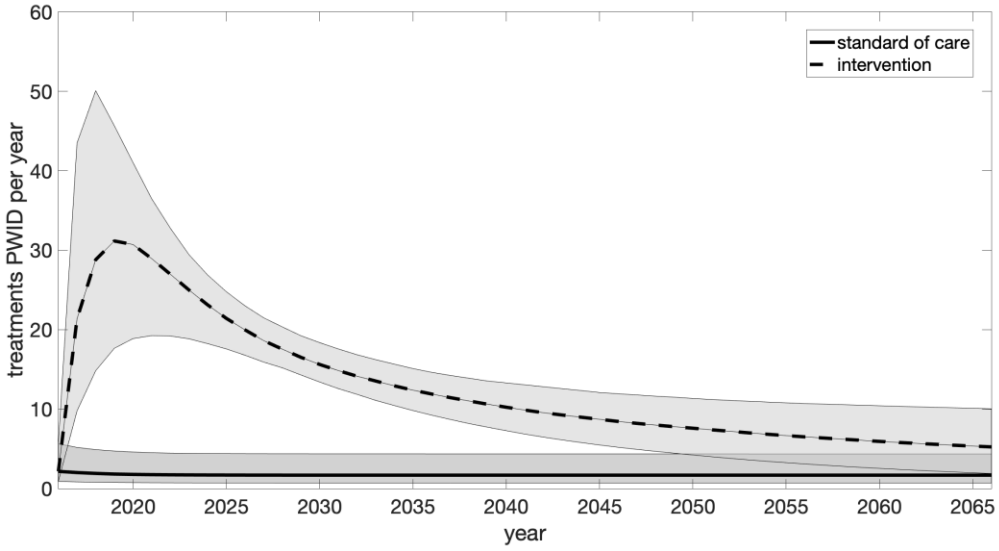
The cost of engagement was calculated using the number of referrals and number of engagements at each site. Nurse facilitators were interviewed to determine proportion of their time spent on research related, managerial or admin, training, diagnosis or engagement tasks. The total cost of engagement included buddy and peer volunteer time as well as expenses. The nurse and key worker staff time was divided by the number of referrals plus volunteer time divided by the number of engaged. To calculate engagement costs for those who were known positives the staff time cost for testing interview was used, as well as the engagement cost, to include the initial consultation time before the referral process is started.

Table S9: Detailed costing inputs for the model – all costs in the table were inflated to 2018 prices after the analysis

Step		Standard of care Cost	Intervention Cost	Source
HepCATT startup cost for first year		0	£24,854-£33,962	HepCATT costing analysis
Second and Subsequent Years fixed costs for HepCATT		0	£10,715-£13,519	
Costs per Test (includes staff time and test costs)	Ab negative	£45 (staff cost)+ £7.4 (Ab test cost) +/- 10%	£104-£158	(11) and HepCATT costing analysis (see supplementary information)
	Ab positive	£45+£7.4+£64.2 (RNA test cost) +/- 10%	£147 - £207	
	Previous known SVR (Ab+)	£45+£64.2+/- 10%	£143 - £203	
Costs per Engagement (includes staff referral costs and preliminary blood tests and fibroscan at the hospital)	From Diagnosed	£325.84 +/- 10% (at hospital)+£75 (referral cost)	£121 - £207 (referral cost) +£325.84±10% (at hospital)	Standard-of-care referral costs from (11), hospital costs from expert opinion (correspondence Graham Foster) Intervention referral costs from HepCATT costing analysis (see supplementary information)
	From Lost to Follow Up	0 (no engagement from lost to follow up for standard-of-care)	£94-£ 121 (identifying patient) +£121-£207 (referral cost) +£325.84±10% (at hospital)	
Cost per Treatment	Treatment Monitoring	£385.04 +/- 10%	£385.04 +/- 10%	Expert opinion (correspondence G Foster and supplementary information for details)
	Weekly Drug Cost	£3,310 +/- 10%	£3,310+/- 10%	Assume full current list price (48)

Figure S1: Model projections of treatments undertaken in PWID (a) and ex-injectors (b) since 2016 with and without the HepCATT intervention. This is for the projections assuming 1000 PWID. The black solid or dashed lines show the median of the model projections with the shaded areas denoting the 95% central range of the model projections.

(a) Current PWID



(b) Former people who inject drugs

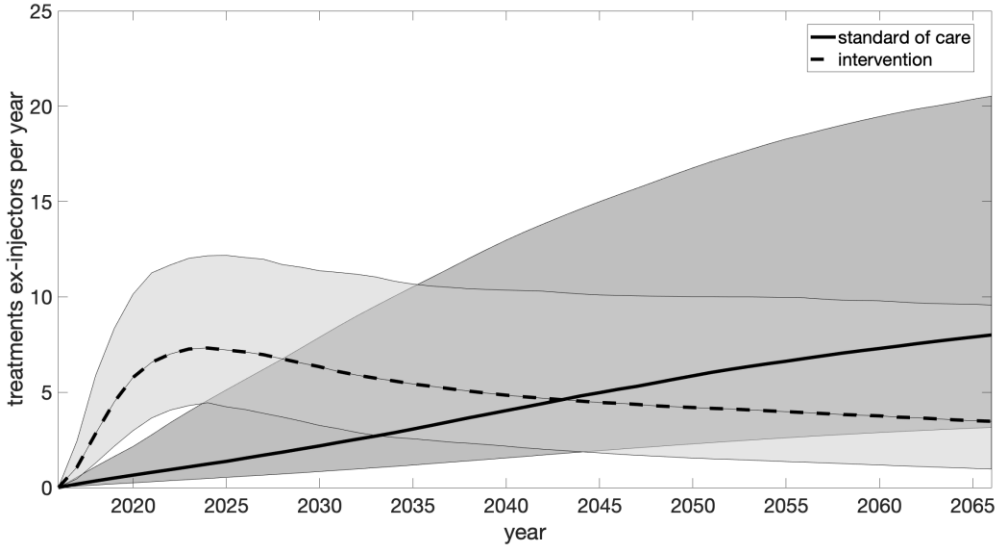


Figure S2 Yearly discounted costs of the intervention and standard-of-care as well as the incremental cost each year.

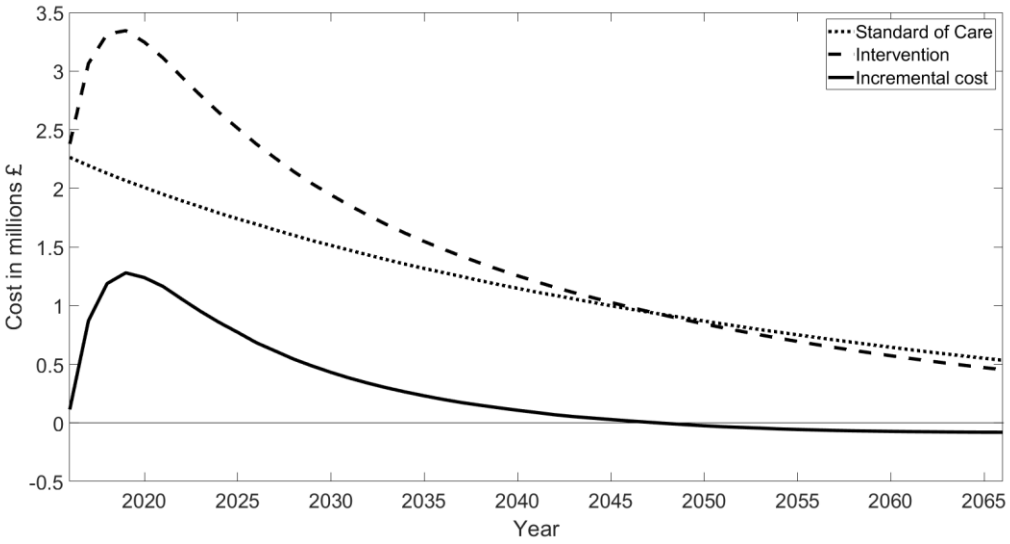


Figure S3 Cost-Effectiveness Plane for HepCATT intervention assuming full list price for HCV treatment and 20% of the full list price. This is for the projections assuming 1000 PWID.

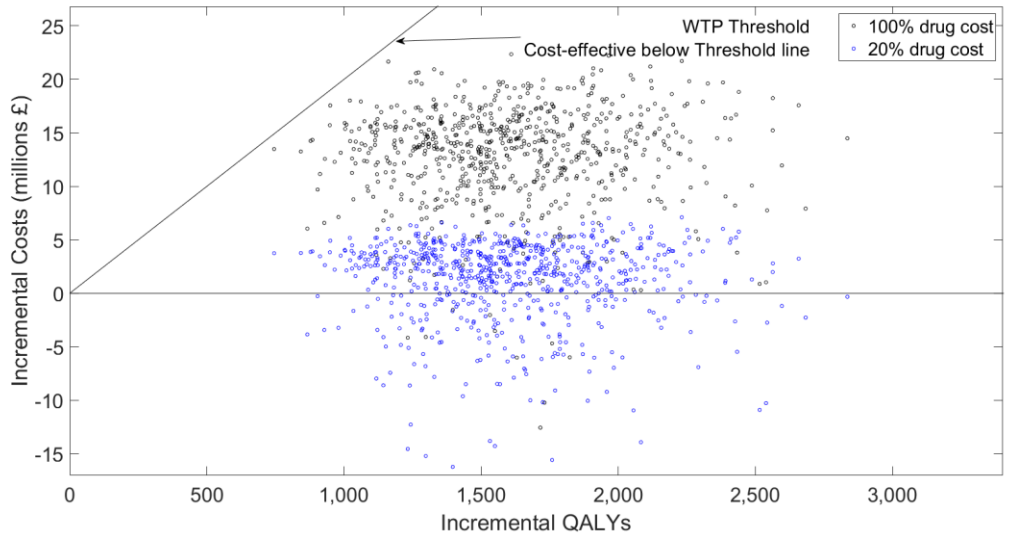


Figure S4 Threshold analysis of mean incremental cost-effectiveness ratio for different drug costs

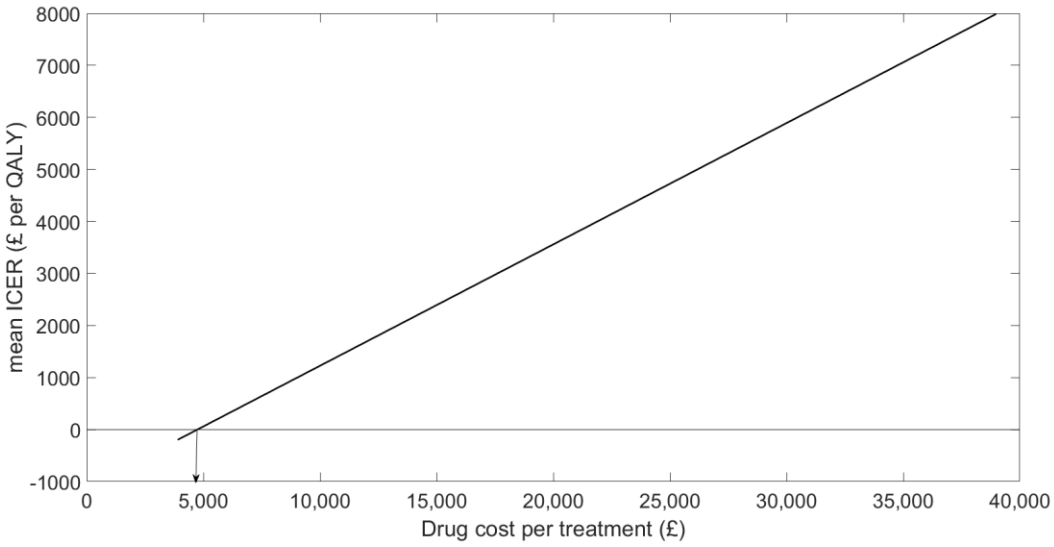


Figure S5 ANCOVA Results: Contribution of uncertainty in each parameter to the variability in the results. Parameters accounting for more than 3% of the uncertainty are shown individually**.**