Sweeney, S, Ward, Z, Platt, L, Guinness, L, Hickman, M, Hope, V, Maher, L, Iversen, J, Hutchinson, SJ, Smith, J, Ayres, R, Hainey, I and Vickerman, P

Evaluating the cost-effectiveness of existing needle and syringe programmes in preventing Hepatitis C transmission in people who inject drugs

TITLE PAGE

EVALUATING THE COST-EFFECTIVENESS OF EXISTING NEEDLE AND SYRINGE PROGRAMMES IN PREVENTING HEPATITIS C TRANSMISSION IN PEOPLE WHO INJECT DRUGS

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ABSTRACT

Aim To evaluate the cost-effectiveness of needle and syringe programmes (NSPs) compared to no NSPs on hepatitis C virus (HCV) transmission in the United Kingdom.

Design Cost-effectiveness analysis from NHS/ health-provider perspective, utilising a dynamic transmission model of HCV infection and disease progression, calibrated using city-specific surveillance and survey data, and primary data collection on NSP costs. The effectiveness of NSPs preventing HCV acquisition was based on empirical evidence.

Setting UK settings with different chronic HCV prevalence among people who inject drugs (PWID): Dundee (26%), Walsall (18%), and Bristol (45%)

Population PWID

Interventions Current NSP provision is compared to a counterfactual scenario where NSPs are removed for 10 years and then returned to existing levels with effects collected for 40 years.

Measurements HCV infections, and cost per quality adjusted life year (QALY) gained through NSPs over 50 years

Findings Compared to a willingness-to-pay threshold of £20,000 per QALY gained, NSPs were highly cost-effective over a time-horizon of 50 years and decreased the number of HCV incident infections. The mean incremental cost-effectiveness ratio was cost-saving in Dundee and Bristol, and £596 per QALY gained in Walsall, with 78%, 46% and 40% of simulations being cost-saving in each city, respectively, with differences driven by coverage of NSP and HCV prevalence (lowest in Walsall). Over 90% of simulations were cost-effective at the willingness-to-pay threshold. Results were robust to sensitivity analyses including varying the time-horizon, HCV treatment cost and numbers of HCV treatments per year.

Conclusions We projected NSPs avert HCV infections and are highly cost-effective in the UK and could be cost-saving to the NHS and other health care providers. NSPs will remain cost-effective in the UK irrespective of changes in HCV treatment cost and scale-up, meaning that NSPs will continue to be an efficient strategy for preventing HCV transmission in the future.

Abbreviations:

HCV, Hepatitis C Virus; PWID, People who inject drugs; NSP, Needle and syringe programmes; IPED, image and performance enhancing drugs; OST, opioid substitution therapy; HCNSP, high coverage needle and syringe provision; QALY, quality adjusted life year; ICER, incremental cost effectiveness ratio; WTP, willingness to pay; NMB, Net monetary benefit; HIV Human Immunodeficiency Virus

MAIN TEXT

INTRODUCTION

Hepatitis C virus (HCV) is a global public health issue, with an estimated 71 million people living with HCV[1, 2]. In the UK, approximately 200,000 are chronically infected, with 90% of new infections occurring among people who inject drugs (PWID)[3, 4]. Similar epidemics exist in other high-income settings[5]. To reduce the burden of HCV, it is crucial to reduce the incidence of HCV among PWID[6].

In most settings, needle and syringe programmes (NSPs) are the primary intervention for reducing the transmission of blood borne viruses among PWID. NSPs provide sterile needles, syringes, injecting equipment, and other prevention and support services. There is good evidence that NSPs reduce injecting risk behaviours, and can prevent the acquisition of HCV and HIV amongst PWID[7-13].

Previous research has shown that NSPs are a cost-effective intervention to reduce HIV incidence in multiple settings[14-21]. However, only two studies have considered their cost-effectiveness in reducing HCV incidence[22, 23], with no studies from western Europe. In the UK, funding for NSPs is under threat due to budget cuts and shifting emphasis of drug policy to recovery and abstinence-based treatment programmes[24]. To improve the evidence base and inform policy choices, it is therefore important to assess the cost-effectiveness of NSP. We evaluated the cost-effectiveness of current levels of NSP provision on the transmission and disease burden of HCV in three UK settings, compared to a counterfactual of no NSP provision.

METHODS

Setting and Intervention

The intervention considered was needle and syringe distribution services to prevent HCV transmission. NSPs in the UK can be provided through several modalities, including pharmacies, mobile vans, or fixed sites. The cost-effectiveness analysis focused on three settings in the UK: Bristol, Dundee and Walsall. These settings were selected based on differences in HCV prevalence, access to intervention coverage data, and feasibility of conducting a cost-effectiveness analysis. Table 1 summarises key attributes of these settings. The chronic prevalence of HCV in the three settings (18-45%) ranges across the UK average of 40%[3]. Coverage of harm reduction interventions varies from 72-81% for opioid substitution therapy (OST) and 30-57% for high coverage needle and syringe provision (HCNSP, taken to be at least one clean needle for every injection) compared with an average of 65% for OST and 48%-77% for HCNSP across UK[3, 25]. Although data is limited, PWID size estimates across our cities (750-2295) suggest they have moderate sized injecting populations[26, 27].

We collected cost data from NSP in each area. We only considered needle and syringe distribution to people who inject psychoactive drugs (such as opioids and stimulants; now denoted as PWID), not those injecting image and performance-enhancing drugs (IPEDs), as they have greater risk of HCV infection[28]. Other services provided by NSPs were not considered, including HCV testing, condom provision, and referral to community drug treatment programmes. In addition, we do not consider the impact of NSPs on HIV transmission.

[Insert Table 1]

Estimation of Costs

The cost-effectiveness analysis uses a UK NHS (health and social care provider) perspective[29]. We estimated the incremental economic cost of NSP provision in each area for 2013-2014[30] in 2014 pounds sterling (GBP). Cost data collection took place between March 2014 and July 2015 at several sites in each city, including the fixed-site NSP, two randomly selected pharmacy-based NSPs, and any additional NSP modalities operating in the area. Costs were estimated for the 2013-14 financial year. We took a bottom-up approach in collecting cost data, first estimating resource use and then valuing those resources according to their opportunity cost[31]. Resource use was measured using direct observation and reviewing programme records. We incorporated all resources: staff salaries, training, equipment, supplies, utilities, and building costs. Current market prices (2014 GBP) were applied to all resources; we estimated a 'shadow cost' for volunteer time or subsidized equipment. Overhead and support costs were estimated from programme records, and a portion allocated to NSP provision based on building space and management/support time. Human resource use was estimated through interviews and direct observations. Research costs were not included. All interviewees provided written consent, and the study received ethical approval by the London School of Hygiene and Tropical Medicine Research Ethics Committee (Reference: 6527).

Cost inputs were defined as fixed costs (do not vary with output) and variable costs (vary with the level of output). Total costs for 2014 were estimated including all NSP modalities in each area, using their total fixed costs, plus an average variable cost for sterile injecting equipment (estimated per needle distributed to PWID).

The costs of HCV care for HCV-related disease came from published estimates for the UK (Table S1)[32, 33], inflated to 2014 prices[34]. We assumed HCV treatment delivery costs for people currently injecting were 20% higher than for ex-injectors (extra nurse time)[35], and assumed treatment with 12-week direct acting antiviral (DAA) regimens after 2016[36] at a total drug cost of £39,600[37](Table S1). We assumed an annual cost for OST[38].

Model Description for Estimating Impact and Cost-effectiveness

A dynamic model of HCV transmission and treatment was developed to estimate the impact of needle and syringe distribution in each city; described elsewhere[10] and in the supplementary materials. Briefly, the model incorporates HCV transmission among PWID and disease progression in PWID and ex-injectors. The model is a deterministic compartmental model using ordinary differential equations, stratified by injecting duration, intervention status (OST and/or NSP, or not), risk status (homeless and/or crack injecting or not), currently injecting or not, infection status and disease stage. New initiates to injecting are initially susceptible to HCV and become infected at a per-capita rate depending on their intervention state, injecting duration category, risk category and prevalence of HCV infection in the population. Risk, whether increased (injecting duration and high-risk categories) or decreased (if on OST and HCNSP), is assumed to apply both to HCV transmission and acquisition. We assume random mixing between all subgroups. The model includes HCV disease progression (Fig 1)[39]. Following successful treatment (sustained viral response), continued slower progression occurs among those with compensated cirrhosis or more severe disease[40-42]. We account for re-infection amongst PWID and re-treatment.

[Insert Figure1]

Model parameterisation and calibration

Epidemiological, demographic and harm reduction related parameters common to both the intervention and counterfactual scenarios for all three cities are in Table S2. The model was further parameterized for each city using context-specific survey data and data from the literature, and calibrated using intervention coverage and HCV prevalence data in three steps. Firstly, the model was calibrated to PWID population size estimates using a PWID demographic sub-model without infection by varying the numbers initiating injecting each year and cessation rates. Secondly, the coverage of HCNSP and OST were fitted using a sub-model that includes HCV transmission but no disease progression (allowing recruitment rates onto HCNSP and OST to vary). Thirdly, the HCV prevalence was fitted using the full model with disease progression by varying the transmission rate for those with no increased or decreased risk (see supplementary information for more details). Additional HCV prevalence and incidence data were used to validate the model projections (Tables S2, S3 and Fig S1). Based on a recent pooled analysis of UK and Australian data, currently being on HCNSP or OST were assumed to reduce the risk of HCV transmission by 41% and 59%, respectively[30], with the risk reduced multiplicatively for those on OST with HCNSP. Service data on the number of needles and syringes distributed in 2014 were used to estimate the proportion of injections utilising sterile injecting equipment (coverage) per PWID in each area to proxy the proportion of PWID on HCNSP. Survey data was used to estimate the proportion of PWID currently on OST.

The model was used to estimate the number of new infections and person-years spent in each HCV disease stage. Quality adjusted life year (QALY) utility weights came from the literature (Table S3)[32, 33], with the baseline quality of life for PWID being lower (0.85) than for other individuals (0.94)[33].

For 2014, the model directly used the total estimated area-level costs of NSP. For other years, total annual costs were adjusted for changes in the number of PWID while assuming the same NSP cost (inflation adjusted) and coverage. Costs of HCV care and treatment were attached to each HCV disease stage. We assumed that half of all mild or moderate patients are diagnosed[3] and incur a cost, whereas all individuals in more progressed disease stages incurred care costs. All costs and QALYs were discounted at 3.5% per year[29].

To reflect parameter uncertainty, distributions were assigned to many model and cost parameters, which were randomly sampled to obtain 1000 model fits (see supplementary materials).

Cost-effectiveness analysis

For the NSP intervention scenario we assumed the coverage of HCNSP remained stable for 50 years (2016-2065). In contrast, the counterfactual scenario ('no NSP') removed the costs and benefits of HCNSP for 10-years (2016-2025), and then re-instated them for 40 years (2026-2065) to capture the future effects of the lack of HCNSP on HCV transmission and disease morbidity. A time-horizon of 50 years is standard practice to consider the lifetime of individuals impacted by the intervention and to fully capture the effects of HCV disease progression[29]. The incremental costs, disease outcomes and QALYs of NSPs compared to 'no NSPs' were estimated over 2016-2065 for all 1000 model fits. Mean incremental cost effectiveness ratios (ICER=incremental costs/incremental effects) were compared to the £20,000 per QALY willingness-to-pay (WTP) threshold recommended by NICE[43]. Mean net monetary benefit (NMB = (incremental effectiveness*WTP threshold)-incremental costs) was also estimated for each area. Cost-effectiveness acceptability curves were plotted to determine the proportion of simulations that are cost-effective at the WTP threshold.

Sensitivity analysis

We carried out multiple sensitivity analyses to test the impact of assumptions on the ICER. These included assuming: no diagnosis for pre-cirrhotic chronic HCV disease (50% diagnosed in main analysis); same HCV treatment cost for people currently and no longer injecting (increased cost for people currently injecting in main analysis); 0% discount rate for costs and QALYs (3.5% in main analysis) and increased time-horizon of 100 years (50 years in main analysis). A threshold analysis also considered the minimum time-horizon over which NSP are cost-effective at a WTP threshold of £20,000 per QALY. To assess the likely impact of the changing landscape of HCV treatment we conducted analyses assuming 50% or 75% lower cost of HCV treatment from 2016; doubling and quadrupling the low HCV treatment rates in

Bristol and Walsall from 2016 (Dundee already has a high treatment rate); and quadrupling the treatment rates in Bristol and Walsall from 2016 while also reducing HCV treatment costs by 75%.

A linear regression analysis of covariance [44] was undertaken to determine which parameter uncertainties contributed most to variability in incremental costs and QALYs.

RESULTS

Cost Analysis for NSP

The size and cost of NSPs varied across the areas (Table 2), as did the number of needles distributed per PWID (Tables S4, S5). Although the annual fixed costs of NSPs varied (£35,983-£49,143 in Bristol to £8,672-£11,807 in Dundee), the average variable cost of injecting equipment was more consistent (median £0.26/needle in Bristol; £0.78/needle in Dundee). Overall, total estimated costs for 2014 range from a median of £79.45/PWID in Walsall to £159.21/PWID in Dundee. Uncertainty in NSP costs were largely driven by assumptions on the wastage of injecting equipment (Fig S2).

[Insert Table2]

Impact projections for NSP

Compared to the counterfactual of no NSP over the next 10 years, projections suggest a median of 84-199 infections (8% of infections in Bristol and Walsall, 40% in Dundee) and 2-20 deaths (1% of deaths in each area) would be averted in each area by continuing provision of NSP over this period, with benefits tracked over a further 40 years. Area-level differences in infections averted are due to variations in HCV treatment coverage (greater in Dundee), with wide uncertainty around the impact projections for each area being due to uncertainty in many model parameters, as discussed later. Despite this uncertainty, all simulations projected deaths and infections averted for the NSP intervention scenario(Table S6).

Cost-effectiveness analysis

In all three settings, over the 50-year time-horizon, healthcare and treatment costs are lower in the baseline NSP scenario than in the no NSP counterfactual scenario (Table S7). Overall, the NSP scenario is cost saving in Bristol and Dundee, saving an average of £159,712 in Bristol and £2.5 million in Dundee over 50-years and gaining 502 and 195 incremental QALYs,

respectively (Table 3). In Walsall, the mean incremental cost of the NSP scenario is £114,442 and gains 192 incremental QALYs (ICER £596 per QALY gained). Using a willingness-to-pay (WTP) threshold of £20,000 per QALY gained[29], this represents a NMB of £10.2 million in Bristol, £6.4 million in Dundee and £3.7 million in Walsall over 50 years.

[Insert Table3]

In each city, all simulations suggest the NSP scenario gains QALYs compared with the no NSP scenario. In Dundee, most simulations (78%) suggest that NSP is cost saving; for Bristol and Walsall, 46% and 40% of simulations respectively are cost saving (Fig 2 and S3). Over 90% of simulations for each area are below the WTP threshold of £20,000 per QALY saved(Fig 2).

[Insert Figure 2]

Sensitivity analysis

The sensitivity analyses indicated that our cost-effectiveness projections are robust to variations in parameter assumptions (Fig 3). Increasing the time-horizon to 100 years made the NSP scenario cost saving in all three cities, as did reducing the discount rate to 0% (costs and QALYs). The threshold analysis revealed that NSP becomes cost-effective in Bristol and Walsall if the time horizon is longer than 2- or 6-years post-intervention, respectively, while in Dundee it is cost-saving even with no years of follow-up.

The highest ICERs for all three settings occurred when the cost of HCV treatment was reduced by 75% (Bristol and Walsall: £1518 and £2812 per QALY respectively, Dundee still cost-saving), but the mean ICERs remained well below the WTP threshold. Quadrupling the treatment rate improved the NSP ICER because of an added prevention benefit in terms of reducing re-infections after successful HCV treatment (All three are cost-saving).

[Insert Figure 3]

Analysis of covariance (Fig S4) suggests that most of the variability in the incremental costs and QALYs in each setting is due to uncertainty in the efficacy of HCNSP (accounting for 52%,

50% and 27% of the variability in incremental costs and 80%, 73% and 20% of variability in incremental QALYs in Bristol, Walsall, and Dundee, respectively). The more effective HCNSP is at reducing HCV transmission the lower the incremental costs and higher the incremental QALYS (see Fig S5 for Bristol example). In Dundee, uncertainty in the prevalence of HCV also caused considerable variability (57% for incremental costs and 61% for incremental QALYs). A higher initial HCV prevalence results in lower incremental costs and higher incremental QALYS resulting in NSP being more cost-effective(see Fig S5). Otherwise, uncertainty in the cost of injecting equipment in Bristol and Walsall was an important cause of variability in incremental costs (10% and 28% respectively), while uncertainty in the coverage of HCNSP was an important cause of variability in the incremental QALYs for Bristol and Walsall (9% and 5% respectively).

DISCUSSION

Main Findings

Our analyses suggest that NSPs are highly cost-effective in the UK, and in some settings cost-saving. We found variation in NSP costs across the three areas; there is no 'standard' structure for NSP services in the UK, and as such, each area had different service modalities and organisational structures. Differences in cost-effectiveness were also driven by variations in the impact achieved; fewest deaths were averted in Walsall due to its lower HCV prevalence[10], whilst more deaths and infections were averted in Bristol due to the higher HCV prevalence and larger PWID population. The largest proportion of infections averted was in Dundee where there is higher coverage of HCV treatment with HCNSP preventing re-infection. These differences did not affect our finding that NSPs are highly cost-effective. Our results were also robust to varied assumptions, including a lower cost for HCV treatment and a scale-up in HCV treatment, both of which are likely to occur in the near future.

Comparison with Existing Evidence

This is the first study evaluating the cost-effectiveness of NSPs in western Europe, and the first ever study to use empirical estimates of the efficacy of NSP for reducing HCV transmission risk[9]. Two other studies have considered the cost-effectiveness of NSP for averting HCV transmission; a study from Baltimore[22] estimated a cost of several hundred thousand dollars per averted HCV infection, and an Australian study indicated that NSPs are cost-saving in preventing HIV and HCV infection due to averted healthcare costs[23]. Unfortunately, it is difficult to compare these findings to our projections. The US study did not collect primary cost data, but assumed a cost of US$5 per NSP client per day, contrasting with our estimates of £0.16-£0.42 per PWID per day. The results of the Australian analysis were driven by the reduction in HIV transmission, which we did not include in our analysis.

Strengths and Limitations

A strength of our analysis lies in our use of primary cost data to reflect the 'real-world' costs of implementing NSPs in the UK. Although this ensures their relevance to the UK, uncertainties still existed due to gaps in the data. This was especially true for pharmacy-based NSP services, where detailed records were not available. These uncertainties in the cost of NSPs were included in our projections, and our findings were robust (i.e. were all cost-effective) despite this. Standardised reporting of number of visits and numbers of needles and syringes distributed would facilitate comparison across different NSP sites, while implementing a system to record the number of individual clients reached would greatly facilitate estimation of unit costs and intervention coverage.

A second potential weakness is that the assessment of health impact is based on model projections rather than study outcomes, and so caution is advised in the interpretation of our cost-effectiveness findings. This is common to all NSP evaluations, with our study improving on previous analyses by using empirical effect estimates for how NSP reduces HCV transmission risk rather than relying on self-reported behaviour change. We incorporated uncertainty in these empirical effect estimates in our analysis, as well as other parameters, which contributed to the large variation in both incremental costs and QALYs. Uncertainty in the HCV prevalence in Dundee also contributed to the variation in incremental costs and QALYs in that setting. Despite this uncertainty, our results were robust, with over 90% of simulations under the UK willingness-to-pay threshold of £20,000 per QALY.

Thirdly, there was uncertainty in the NSP coverage for each area. We used conservative service provision estimates of NSP coverage, which were lower or comparable to survey estimates from each setting, and also included uncertainty around these coverage estimates. More accurate estimates of syringe coverage are needed, as is consistent monitoring of NSPs and the services they provide[12].

Our approach to estimating the cost-effectiveness of NSPs was highly conservative: we did not incorporate other potential health benefits of NSP, or impact on people injecting IPEDs. We did not incorporate the health benefits associated with NSPs reducing the risk of HIV acquisition[45] because of difficulty in reliably modeling the transmission of an infection that is at low-levels. Incorporating HIV infections averted would improve our cost-effectiveness estimates[15, 46]. The analysis also did not include the health benefits from reducing injection-site infections and injuries [47], which may result through engaging the client in discussions about safer injecting behaviour. Our analysis also did not reflect the potential impact of NSPs in addressing the complex mental health and social support issues that PWID experience[48, 49]. When considering other potential benefits of NSPs, such as preventing HIV infection or skin and soft tissue infections, and addressing the psychosocial and welfare needs of PWID, NSPs are likely to be highly cost-saving.

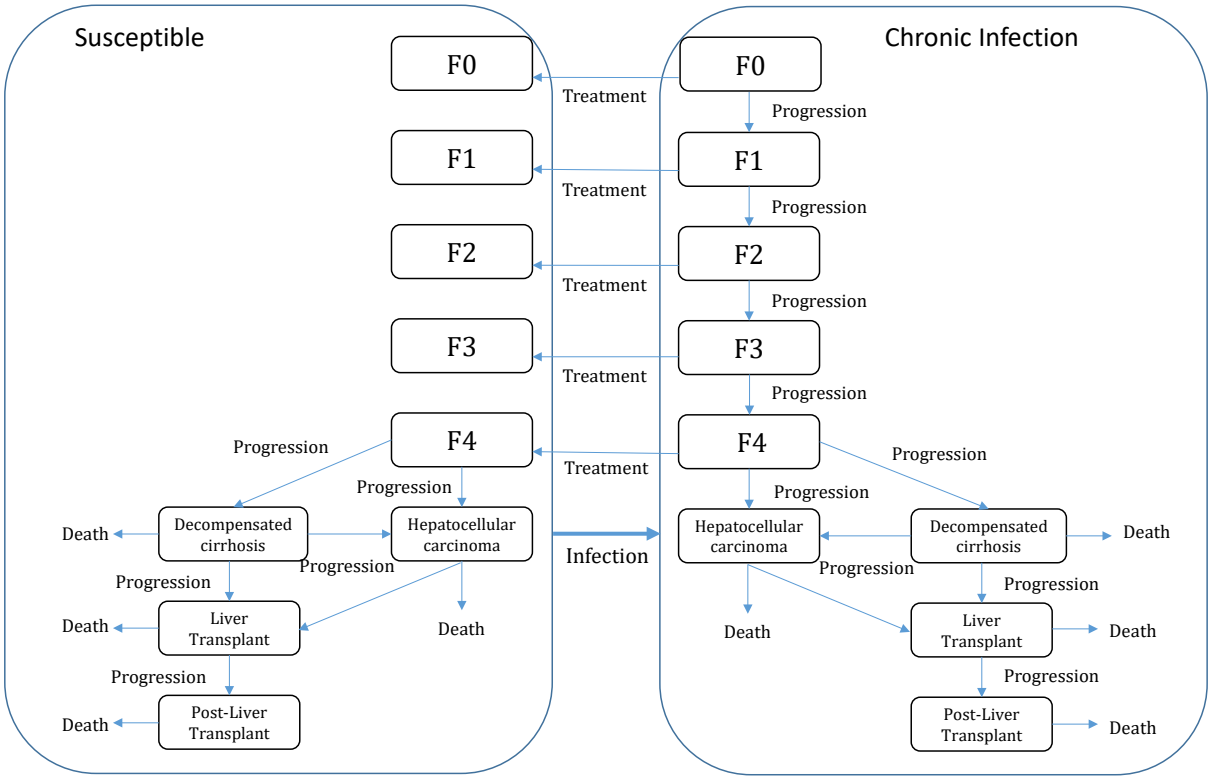
Implications and conclusions

NSP services are a highly effective low cost intervention to reduce HCV transmission, and in some settings are cost-saving. For example, in Dundee, we estimate long-term savings of up to 250% of the initial investment. In a recent analysis of public health interventions considered by NICE between 2006 and 2010, only 15% were cost-saving[50]. In this context, NSPs can be considered a very strong investment choice.

These findings clearly point to the need to maintain funding for NSP services in the UK and elsewhere – while at the same time emphasising the need to strengthen the evidence for their effectiveness, including how the level of NSP provision and other NSP characteristics affect its efficacy. Further work should also investigate what strategies or factors improve the cost-effectiveness of NSP and what can aid its scale-up. The findings also highlight the importance of joint commissioning and decision-making between agencies in the UK to meet the needs of local populations. Due to recent NHS reforms, the agencies responsible for commissioning NSPs are often different from those incurring any cost-savings. A co-financing approach would better represent the overall societal benefits of such an investment[51]. Different agencies may also need outcomes on different time frames; a lifetime horizon is recommended in NICE guidance for economic evaluations, while policy-makers and funders are more concerned with short-term outcomes. We found that shorter time-horizons remained cost-effective in Bristol and Walsall (after 2- and 6-years of follow-up), and cost-saving in Dundee. Short-term returns may also be accrued through psychosocial and welfare benefits of NSPs as mentioned above.

These findings, whilst having limited generalisability for low and middle-income countries, are likely to be highly generalisable to other high-income settings with comparable HCV prevalence and harm reduction coverage such as Australasia and Western Europe[52], and therefore support the recommendations of WHO to develop and implement policies to support harm reduction among PWID[53]. These interventions should be delivered in combination with and complemented by prioritisation of drug treatment and expansion of HCV and HIV treatment[24].

Fig 1 Disease progression model



F0-F4 are Metavir liver disease stages, with F0-F1 being mild disease, F2-F3 being moderate disease and F4 being compensated cirrhosis. Progression through the disease states occurs at a rate determined by the current disease state, as are the disease related death rates. All states have a cessation rate from injecting drug use and a non-disease related background death rate. Infection can occur from all disease states but are not shown for clarity. Those who spontaneously clear the infection are assumed to remain in the susceptible category.

Table 1 Coverage of OST and NSP and epidemiology of HCV among PWID in each city in 2014

Baseline Characteristics	Bristol	Dundee	Walsall
PWID population size (2011)	2295 (2025-2564) [a]	750 (675-825) [b]	1460 (1296-1623) [c]
Total adult population size (aged 15-59)[54]	286,000	99,000	170,898
Prevalence of current injecting drug use in adult population (%)	0.8	0.75	0.85
Chronic HCV Prevalence in PWID population	45% (40-50%) [d]	26% (19-32%) [e]	18% (11-26%) [d]
Proportion of PWID on OST	81% (77-86%) [f]	73% (65-79%) [e]	72% (61-82%) [d]
Proportion of PWID with HCNSP (from service provision calculation)	57% (38-82%) [d]	49% (34-79%) [e]	30% (21-42%) [d]
Number PWID treated for HCV per year	18 [g]	40 [h]	2 [i]

[a] adjusted from [26]; [b] local estimate adjusted from [27]; [c] unpublished PWID prevalence for West Midlands; [d] Data extracted from unlinked anonymous monitoring survey [4]; [e] data extracted from Needle Exchange Surveillance Initiative [55]; [f] Mills, 2012 [56]; [g] Martin, 2015 [57]; [h] from 2015, personal communication John Dillon (Professor of Hepatology and Gastroenterology); [i] assumed similar rate per infected PWID as Bristol as conservative estimate; HCNSP high coverage needle and syringe provision; PWID people who inject drugs; OST, opioid substitution therapy; HCV, hepatitis C virus

Table 2 NSP related costs for PWID by city in 2014 GBP: Inputs for the model

City	Total Needles distributed			Total Annual Fixed Costs			Average Variable Cost per Needle			Total Annual Cost		
	Median	Min	Max	Median	Min	Max	Median	Min	Max	Median	Min	Max
Bristol	820,593	786,540	844,650	£44,142	£35,983	£49,143	£0.26	£0.15	£0.41	£262,762	£147,761	£391,409
Dundee	142,098	138,250	145,770	£10,159	£8,672	£11,807	£0.78	£0.37	£1.19	£120,797	£62,123	£180,050
Walsall	231,457	225,270	237,110	£21,068	£16,321	£26,319	£0.45	£0.20	£1.03	£110,715	£66,667	£153,667

(for more information on derivation see supplementary information and [30]); NSP, needle and syringe provision; PWID, people who inject drugs.

Table 3 Cost-effectiveness results: average total costs (2014 GBP), QALYs and incremental effectiveness ratios for the baseline NSP scenario compared with the no NSP scenario over 50 years

	Total Cost	Incremental Cost	Total QALYs	Incremental QALYs	Mean ICER	NMB
Bristol						
no NSP	£304,157,179		187,663			
NSP	£303,997,467	-£159,712	188,165	502	dominant	£ 10,201,117
Dundee						
no NSP	£94,951,896		83,904			
NSP	£92,455,470	-£2,496,426	84,099	195	dominant	£ 6,390,222
Walsall						
no NSP	£153,697,867		142,702			
NSP	£153,812,309	£114,442	142,894	192	£596	£ 3,722,890

QALY, quality adjusted life year; ICER, incremental cost effectiveness ratio; NMB, net monetary benefit; NSP, needle and syringe programmes.

Figure 2 Cost-effectiveness acceptability curves for each city

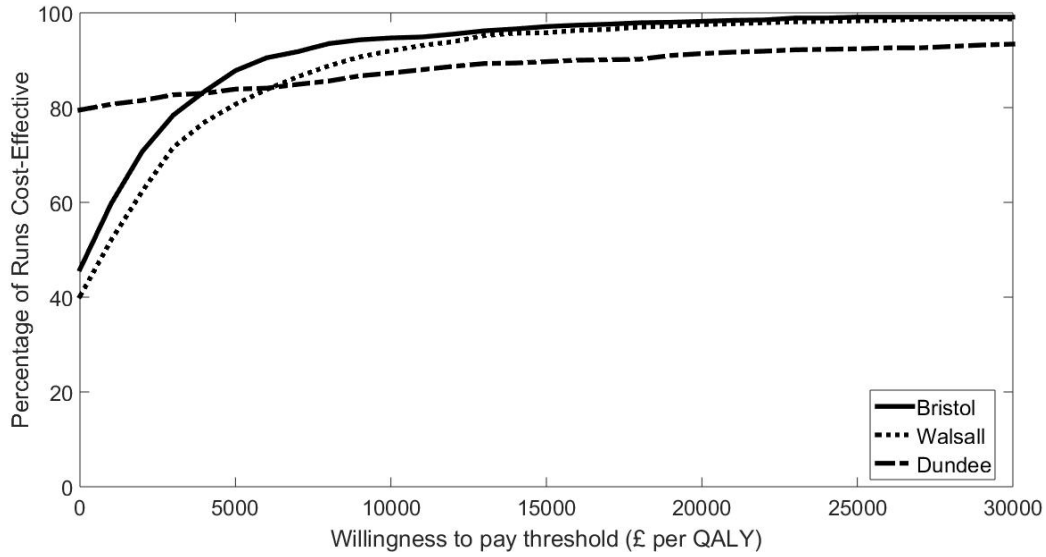
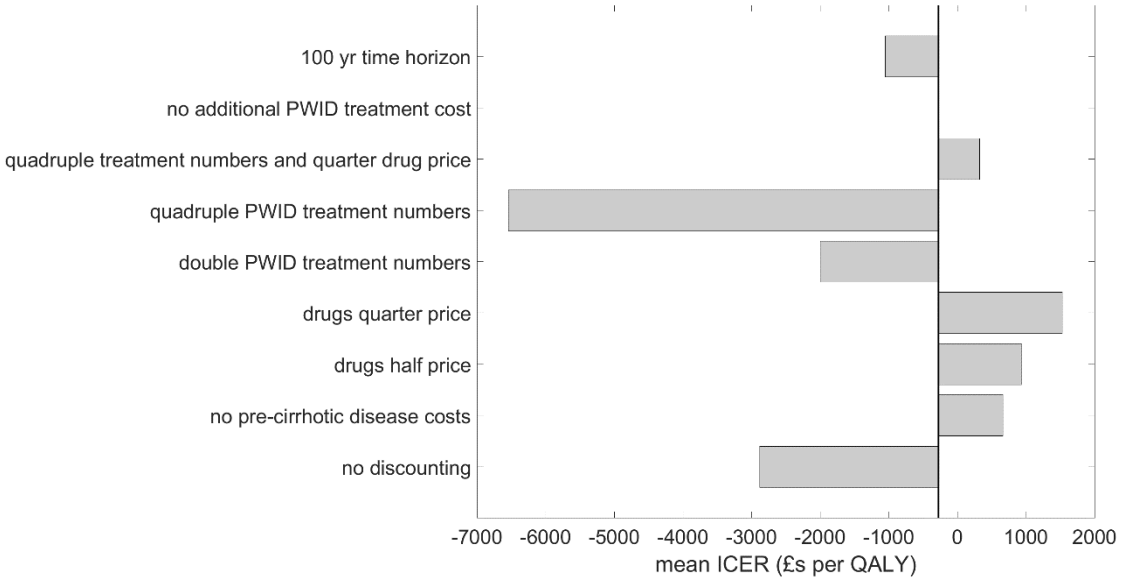
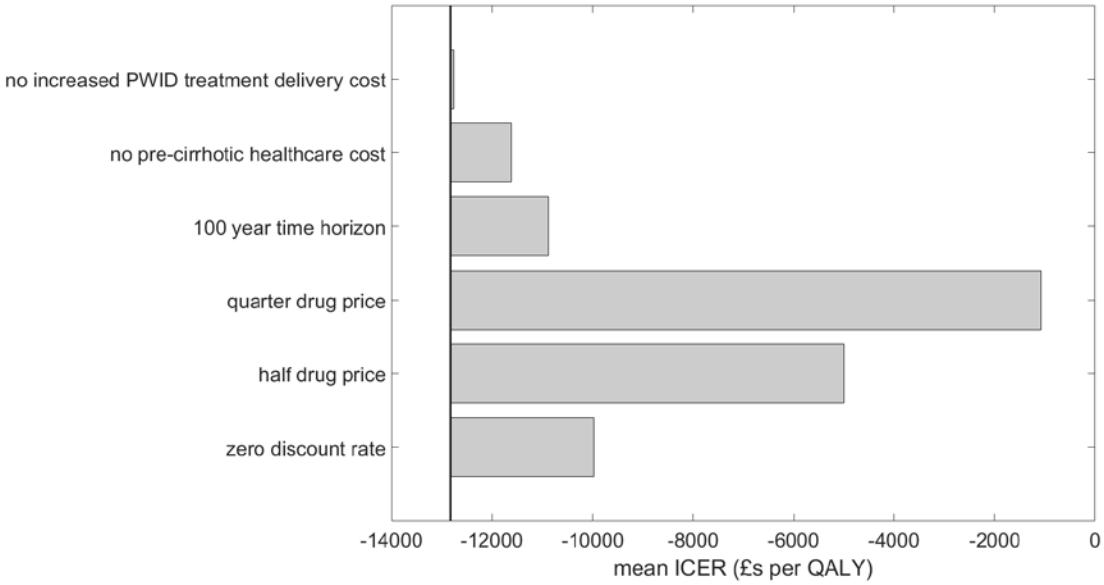


Fig 3 Univariate Sensitivity Analysis

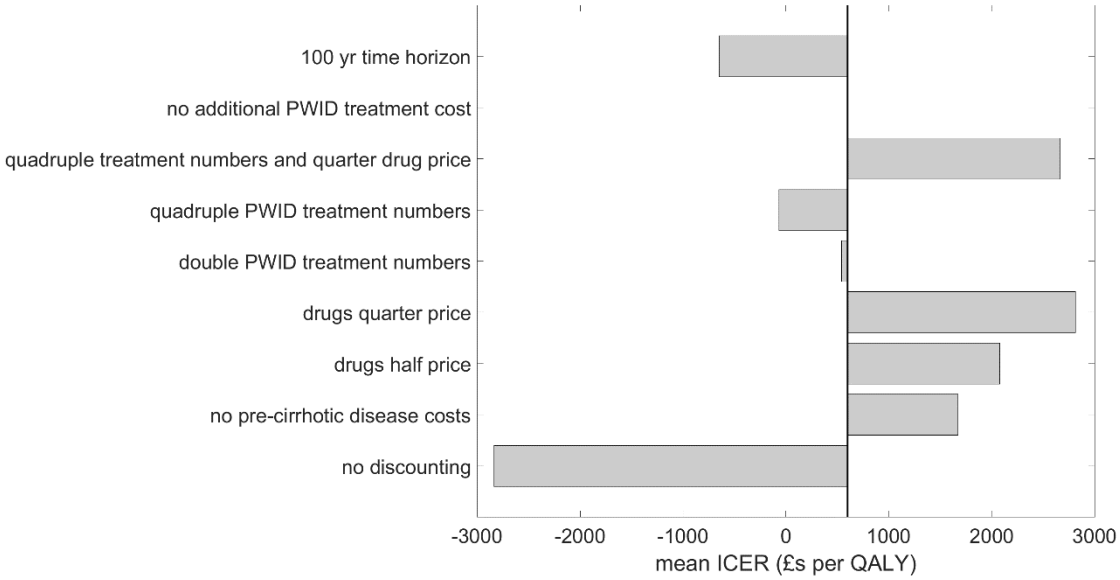
Bristol



Dundee



Walsall



ICER, incremental cost effectiveness ratio; QALY, quality adjusted life year

Supporting Information

S1 Appendix. Technical Supplement

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Supplementary Material

Evaluating the cost-effectiveness of needle and syringe programmes in preventing Hepatitis C transmission in people who inject drugs

METHODS

ESTIMATION OF COSTS

DATA COLLECTION

Data collected incorporates the costs for different modalities of NSP provision (pharmacy, specialised and mobile sites) within each city. Each area provided a different range of modalities. In Bristol, one fixed site NSP which also provided outreach and sub-contracted NSP services to 25 pharmacies. In Dundee, there was one fixed-site NSP and five pharmacies overseen by a team of specialist nurses. Finally, in Walsall there was one fixed-site NSP which sub-contracted to 12 pharmacies, 1 out-of-hours pharmacy, and one drop-in centre. In total, we collected cost data for three fixed sites (one per city), six pharmacies (two per city), and three 'other' modalities (including mobile outreach, out-of-hours pharmacy services, and a drop-in centre), which could potentially enable scale-up of output and coverage levels. Only a sub-sample of pharmacies was costed in detail due to time and cost limitations for the study. The costs of remaining pharmacies in each area were estimated using their output data and unit cost data from the pharmacies where detailed costings were undertaken to give an overall cost estimate per area.

The cost analysis covers a period of one financial year (2013-14), the most recent for which data was fully available, and takes a provider perspective. We estimated the total and unit economic costs for distributing clean needles to people who inject drugs. Our approach to costing was incremental to existing services, and was focused on needle and syringe exchange. We took an ingredients-based approach in costing, first estimating the resources used in delivering NSP services and then applying current market prices (2014 pounds sterling) to all resources in order to estimate a cost. Where the market price did not accurately reflect the value of resources (for example volunteer time), we estimate a 'shadow cost' based on equivalent salary rates for the position in question (1, 2). Overhead and support costs were estimated from programme records, and a portion allocated to NSP services.

In collecting resource use data, where possible, data were extracted from existing reporting mechanisms including budget and expenditure records, human resources records and the management information system. In addition, we carried out direct observations of staff time and activities in order to confirm supply use estimates, and allocate resources which are shared between the NSP and other harm reduction services (such as staff time, building space, equipment or vehicle operation). Shared resources were allocated to services as a proportion of total services delivered and total time spent on each service. Data were collated in a standardized MS Excel spreadsheet. Data collection was primarily conducted by one researcher, and quality-controlled by a second researcher.

Due to the nature of pharmacy-based needle exchange, there was far less detailed output data available within pharmacies. We therefore took a number of assumptions in estimating the outputs at pharmacies. The type of data available for pharmacy-based needle distribution in each city varied; in Bristol pharmacies reported on the total number of visits, while in Dundee pharmacies reported on both the number of visits and the total number of needles distributed. Walsall pharmacies reported on the number of packs distributed. Based on feedback both from pharmacies and fixed sites, we assumed that 100% of clients obtaining needles at pharmacies were opiate users,

and that users of image and performance-enhancing drugs (IPEDs) did not access NSPs at pharmacies. We conducted observations of transactions at six pharmacies, and from these observations assumed that pharmacies distributed an average of 1.12 needle packs per transaction. The out-of-hours pharmacy had begun distribution of 'one-hit kits' shortly before the data collection period; as there was very little information on the quantity of 'one-hit kits' distributed per visit, we varied our assumption of 'one-hit kit' distribution as between 1 and 10 kits per visit – this was drawn from the minimum and maximum quantities distributed per visit in the two weeks prior to the site visit.

Data Analysis

Fixed and Variable costs

Costs at all sites were classified as fixed and variable costs to facilitate analysis. Fixed costs are defined as those costs which are not easily changed in the short-term. Fixed costs included the following ingredients:

- *Overhead costs for pharmacy/ fixed site management*, estimated as the percentage of needle exchange services delivered, as compared to other services delivered in the pharmacy/ in the local area.
- *Coordination by commissioners*, included as overhead and allocated to the site as the percentage of needle exchange services delivered, as compared to other services delivered in the pharmacy/ in the local area.
- *Training* as a minimum includes awareness of the need for discretion, but this should also include an understanding of how to treat people in a non-judgemental way, and may include further education on common injecting practices and harm reduction messages. Training costs were estimated using an ingredients-based approach
- *Health and safety training*, included as a cost for fixed site staff but not for pharmacists, who as a part of their normal job, will already have received health and safety training (e.g. needle stick injuries) and received hepatitis B vaccines
- *Vehicle purchase*, estimated using an ingredients approach, and allocated as the proportion of mileage used for NSP services as compared to other services.

Variable costs are those costs which vary depending on the volume of services provided, and can change in the short-term. Variable costs included in the analysis are:

- *Injecting equipment* in pre-made packs or "pick 'n' mix" as appropriate to the site/service. Equipment and paraphernalia distributed varied between pharmacies and fixed sites and from site to site. *Equipment* distributed includes: pots, water, citric acid, needles/syringes (various types and sized), condoms, sharps bins. The cost of this equipment will be estimated using a combination of the ingredients-based approach and step-down accounting. For pharmacies distributing needle packs, the base case analysis assumes that packs of 10 are routinely distributed. This is varied to packs of 20 needles in the sensitivity analysis.
- *Staff time costs* including service and administrative staff, allocated to NSP services as a percentage of their time use for NSP services as compared to other services, using a combination of observational and interview data
- *Waste management* and disposal of returned needles.
- *Vehicle fuel, insurance and maintenance costs*, estimated using an ingredients approach, and allocated as the proportion of mileage used for NSP services as compared to other services.

Estimating city-level costs

In order to input into the cost-effectiveness model, we estimated the total cost for distribution of needles to people injecting opiate and other non-IPED drugs in each of the three commissioning areas included in the study. We take the assumption that IPED users are at reduced risk of hepatitis C infection via shared needles (3). This is based on low reported prevalence of hepatitis C within IPED users.

Our estimate of total costs for distributing needles to non-IPED users is estimated using total fixed costs at the city level, plus a weighted average variable cost per needle distributed to opiate clients. This estimation approach is intended to proxy the equivalent costs of providing needles only to opiate users; it represents the full fixed cost of the infrastructure necessary to provide needle and syringe exchange and the variable cost attributable to non-IPED users. We anticipate this to be a conservative approach, which does not account for the benefit of distributing needles to IPED users.

Total fixed cost at city level are estimated accounting for the fixed site in each city, as well as all pharmacies and other modalities operating in each city. For pharmacies not included in our costing sample, we estimated an average fixed cost per pharmacy for each commissioning area using the two or three pharmacies sampled for detailed cost data collection. We then applied an average fixed cost to all pharmacies across the commissioning area; this information was provided by fixed sites in each city. Most pharmacies were provided with a small incentive payment per transaction. Where incentive payments were less than or equal to the costs of staff time for transactions these were treated as a transfer, and not included as an additional cost. Where incentive payments were greater than the costs of staff time, any additional amount was considered to be an additional cost and factored into the total cost estimate.

Average variable costs per opiate needle distributed were estimated for each service modality in each city, and weighted to reflect the total proportion of opiate needles distributed through that service modality city-wide. This weighted average variable cost was then applied to the total number of needles distributed city-wide to come to an estimate of the total city-wide variable cost.

In order to understand the impact of uncertainty encountered in collecting NSP costs in the cost-effectiveness model, we conducted a univariate sensitivity analysis. We included factors in the sensitivity analysis which could not be directly observed, or which varied substantially between sites – including supply wastage, staff time taken for needle distribution, volunteer salaries, equipment wastage, opiate/IPED client mix, number of needles distributed per visit, and discount rate. The results from this sensitivity analysis are presented in Supplementary Figure 2. Parameters with the greatest impact on cost at a city level included assumptions surrounding supplies/equipment wastage and personnel time. Reducing estimated supplies/equipment cost by 50% resulted in an average of 26% reduction in city-level costs, while increasing equipment costs to 200% of that observed increased city-level costs by an average of 52%. Reducing staff costs by 50% reduced total city-level costs by an average of 8%, while increasing staff costs to 200% increased total city-level costs by an average of 17%.

TABLE S1 HEALTH RELATED COSTS AND QALY WEIGHTS ASSOCIATED WITH DIFFERENT STAGES OF DISEASE PROGRESSION

	Value £	Distribution	Source
Annual Costs			
OST (specialist prescribing)	2,839.28	Gamma	(4)
Uninfected	0.00	Constant	(5)
F0 and F1 Mild HCV	187.59	Gamma(0.659,289)	(5)

F2 and F3 Moderate HCV	974.68	Gamma(0.485,2038)	(5)
Compensated Cirrhosis	1,546.98	Gamma(0.211,7452)	(5)
Decompensated cirrhosis	12,397.57	Gamma(0.901,13974)	(5)
Hepatocellular Carcinoma	11,170.04	Gamma(0.926,12251)	(5)
Liver transplant	40,273.00	PPIxGamma(89.75,304.5)	(6)
Post-transplant	2,041.00	PPIxGamma(15.22,91.1)	(6)
Hospital costs year of transplant	13,937.00	PPIxGamma(13.78,686.4)	(6)
Treatment			
sofosbuvir + ledipasvir – PWID	48,816.00	Constant	(6)
sofosbuvir + ledipasvir - ex/non-PWID	40,680.00	Constant	(6)
Liver-related death	0.00	Constant	assumption
QALY Weights			
Uninfected			
Ex / non-PWID	0.94	Constant	(6)
PWID	0.85	Uniform (0.8, 0.9)	(6)
Mild HCV			
Without Treatment (F0 and F1)	0.77	Beta (521.2375,155.6943)	(6)
SVR (F1 only)	0.82	Beta (65.8678,14.4588)	(6)
Moderate HCV (F2 and F3)			(6)
Without Treatment	0.66	Beta (168.2461, 86.6723)	(6)
SVR	0.72	Beta (58.0608,22.592)	(6)
Compensated Cirrhosis			
Without Treatment	0.55	Beta (47.1021, 38.5381)	(6)
SVR	0.61	Beta (58.0608,37.1124)	(6)
Decompensated cirrhosis	0.45	Beta (123.75, 151.25)	(6)
Hepatocellular Carcinoma	0.45	Beta (123.75, 151.25)	(6)
Liver transplant	0.45	Beta (123.75, 151.25)	(6)
Post-transplant	0.67	Beta (59.2548, 29.1852)	(6)
Liver-related death	0		(6)

PPI =Hospital and Community Health Services Pay and Price Index Inflation 2003/04 to 2014/2015 (1.47). QALY (quality adjusted life year)

Model Description for Estimating Impact and Cost-effectiveness

Stratifications by injecting duration are included to incorporate increased injecting cessation and HCV-acquisition risk among people recently initiated into injecting(7-9), with the chosen category in line with reporting from the unlinked anonymous monitoring (UAM) survey of PWID (10). PWID are also stratified into different intervention states that influence HCV transmission risk: no intervention, OST only, HCNSP only, or both. PWID enter the model as recent initiates with no intervention coverage. They transition through successive injecting duration categories with rates of injecting cessation and non-HCV related death. *Due to a lack of data, we assumed recruitment and leaving rates onto and off OST and HCNSP were independent of the current intervention state; previous modelling suggests this should not affect our model projections*(11). The model is further stratified by high and low HCV transmission risk, with a proportion starting injecting in the high-risk category(12) and PWID transitioning between these categories. PWID were defined as high-risk if they had been homeless in the last year and/or injected crack in last 4 weeks (low-risk otherwise), which was associated with increased HCV transmission risk(13).

New initiates into injecting are initially susceptible to HCV, and become infected at a per-capita rate depending on their intervention state, injecting duration category, risk category, and prevalence of HCV infection in the population. *Previous analyses suggest incorporating like-with-like mixing (individuals with the same risk behaviour or characteristics being more likely to form injecting contacts with each other than with other individuals) will have little effect on our model projections(11), with data suggesting it only occurs weakly in Bristol(14), and so random mixing was assumed between all sub-groups.*

Once infected, some PWID spontaneously clear infection(15), with the remainder becoming chronically infected, which is life-long unless treated. Chronically infected PWID progress through disease states (Figure 1c*)* with HCV disease-related death occurring from the decompensated cirrhosis, hepatocellular carcinoma, liver transplant and post-liver transplant stages.

HCV treatment is only allowed in the F0-F3 and compensated cirrhosis states as it is unclear whether treatment in later disease stages is beneficial(16). An annual number of PWID are treated, with a proportion achieving a sustained virological response (SVR-effective cure) and the remainder returning to their prior infection category. Following successful treatment, no further disease progression occurs in the F0-F3 states(17, 18), but continued slower progression occurs among those with compensated cirrhosis(18, 19). We allow re-infection of those who have attained SVR, and re-treatment of those who fail treatment or become re-infected in line with current recommendations(20).

Model Equations

$S_{i,j,k}^{n,m}$ and $C_{i,j,k}^{n,m}$ are the number of susceptible and chronically infected individuals in the model, where $i = 0,1$ for off OST and on OST respectively, $j = 0,1$ for <100% NSP and >100% NSP respectively, $n = 1,2,3,4$ for recent and non-recent or long-term injectors and ex PWID, $m = l, h$ for low and high risk respectively and $k = 1,2 \ldots 9$ for the disease progression states chronic infected (F0, F1, F2, F3), compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, liver transplant and post liver transplant respectively.

The ordinary differential equation model is made up of 450 equations which are described below in sections for different aspects of the model.

Inflow of injectors

There are only two variables in the model which allow an inflow of new injectors. These are low and high-risk susceptible individuals in the first disease progression category with no intervention: the number of new low risk individuals per year is $\theta(1-\phi)$ and the number of new high-risk individuals per year is $\theta\phi$.

Injecting duration progression

These terms in the equations are concerned with movement from one injecting duration category to another as well as PWID related and background mortality. $ID_{i,j,k}^{n,m}$ denotes the terms in an ordinary differential equation of injecting duration category n. It occurs for all values of m, i, j, k. $Y_{i,j,k}^{n,m}$ is used to describe one of the variables in the model, where $Y = S$ or C and the subscripts and superscripts are as described previously. The leaving rate, $\mu_i = \omega_i + \nu_i$, where ω_i is the cessation rate and ν_i is the death rate for injecting duration i.

$$\begin{pmatrix} ID_{i,j,k}^{1,m} \\ ID_{i,j,k}^{2,m} \\ ID_{i,j,k}^{3,m} \end{pmatrix} = \begin{pmatrix} -\tau_1 - \mu_1 & 0 & 0 \\ \tau_1 & -\tau_2 - \mu_2 & 0 \\ 0 & \tau_2 & -\tau_3 \end{pmatrix} \begin{pmatrix} Y_{i,j,k}^{1,m} \\ Y_{i,j,k}^{2,m} \\ Y_{i,j,k}^{3,m} \end{pmatrix}$$

When $n = 4$ (ex PWID) the terms have a different form:

$$ID_k^4 = \sum_{i,j,m} \omega_1 Y_{ijk}^{1,m} + \sum_{i,j,k,m} \omega_2 Y_{ijk}^{2,m} + \sum_{i,j,k,m} \omega_3 Y_{ijk}^{3,m} - \nu_4 Y_k^4$$

Interventions: OST and NSP

These terms in the equations are concerned with movement of injectors from one intervention category to another. $IT_{i,j,k}^{n,m}$ denotes the terms in the ordinary differential equation of OST intervention category i and NSP intervention category j. The rates η and β are the recruitment rates onto NSP and OST respectively. The rates κ and γ are the leaving rates of NSP and OST respectively. These terms can be found for all values of m, k and current injector categories but not the exPWID categories ($n = 4$)

$$\begin{pmatrix} IT_{0,0,k}^{n,m} \\ IT_{1,0,k}^{n,m} \\ IT_{0,1,k}^{n,m} \\ IT_{1,1,k}^{n,m} \end{pmatrix} = \begin{pmatrix} -\eta - \beta & \gamma & \kappa & 0 \\ \beta & -\gamma - \eta & 0 & \kappa \\ \eta & 0 & -\kappa - \beta & \gamma \\ 0 & \eta & \beta & -\gamma - \kappa \end{pmatrix} \begin{pmatrix} Y_{0,0,k}^{n,m} \\ Y_{1,0,k}^{n,m} \\ Y_{0,1,k}^{n,m} \\ Y_{1,1,k}^{n,m} \end{pmatrix}$$

High and Low risk

These terms in the equations are concerned with movement of current injectors between low and high risk. $HR_{i,j,k}^{n,m}$ denotes the terms in the ordinary differential equation of risk category m. Here σ is the initiation rate into high risk categories and ζ is the leaving rate. These terms can be found in the equations for all values of i, j, k and $n = 1,2,3$.

$$\begin{pmatrix} HR_{i,j,k}^{n,l} \\ HR_{i,j,k}^{n,h} \end{pmatrix} = \begin{pmatrix} -\sigma & \zeta \\ \sigma & -\zeta \end{pmatrix} \begin{pmatrix} Y_{i,j,k}^{n,l} \\ Y_{i,j,k}^{n,h} \end{pmatrix}$$

Disease progression

These terms in the equations are concerned with movement through the disease states. Infection and treatment are described separately. $DS_{i,j,k}^{n,m}$ denotes the terms in the ordinary differential equation of disease category k for susceptible individuals and $DC_{i,j,k}^{n,m}$ for infected individuals. Below is a description of the rates.

Parameter description	**symbol**
Yearly progression rate from f0 to f1	ρ_1
Yearly progression rate from f1 to f2	ρ_2
Yearly progression rate from f2 to f3	ρ_3
Yearly progression rate from f3 to compensated cirrhosis	ρ_4

Yearly progression rate from compensated cirrhosis to decompensated cirrhosis	ρ_5
Yearly progression rate from compensated cirrhosis or decompensated cirrhosis to hepatocellular carcinoma	ρ_6
Yearly progression rate from decompensated cirrhosis or HCC to liver transplant	ρ_7
Yearly progression rate from liver transplant to post liver transplant	ρ_8
Decompensated cirrhosis related death rate per year	d_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_6
Relative risk for progression rate from compensated to decompensated cirrhosis (ρ_5) following SVR	e_5
Relative risk for progression rate from compensated cirrhosis to HCC (ρ_6) following SVR	e_6

These terms can be found in the equations for all values of i, j, n and m.

$$\begin{pmatrix} DS_{i,j,1}^{n,m} \\ DS_{i,j,2}^{n,m} \\ DS_{i,j,3}^{n,m} \\ DS_{i,j,4}^{n,m} \\ DS_{i,j,5}^{n,m} \\ DS_{i,j,6}^{n,m} \\ DS_{i,j,7}^{n,m} \\ DS_{i,j,8}^{n,m} \\ DS_{i,j,9}^{n,m} \end{pmatrix}$$

$$= \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -e_5\rho_5 - e_6\rho_6 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & e_5\rho_5 & -\rho_6 - \rho_7 - d_6 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & e_6\rho_6 & \rho_6 & -\rho_7 - d_7 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \rho_7 & \rho_7 & -\rho_8 - d_8 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \rho_8 & -d_9 \end{pmatrix} \begin{pmatrix} S_{i,j,1}^{n,m} \\ S_{i,j,2}^{n,m} \\ S_{i,j,3}^{n,m} \\ S_{i,j,4}^{n,m} \\ S_{i,j,5}^{n,m} \\ S_{i,j,6}^{n,m} \\ S_{i,j,7}^{n,m} \\ S_{i,j,8}^{n,m} \\ S_{i,j,9}^{n,m} \end{pmatrix}$$

$$\begin{pmatrix} DC_{i,j,1}^{n,m} \\ DC_{i,j,2}^{n,m} \\ DC_{i,j,3}^{n,m} \\ DC_{i,j,4}^{n,m} \\ DC_{i,j,5}^{n,m} \\ DC_{i,j,6}^{n,m} \\ DC_{i,j,7}^{n,m} \\ DC_{i,j,8}^{n,m} \\ DC_{i,j,9}^{n,m} \end{pmatrix}$$

$$= \begin{pmatrix} -\rho_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \rho_1 & -\rho_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \rho_2 & -\rho_3 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \rho_3 & -\rho_4 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \rho_4 & -e_5\rho_5 - e_6\rho_6 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & e_5\rho_5 & -\rho_6 - \rho_7 - d_6 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & e_6\rho_6 & \rho_6 & -\rho_7 - d_7 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \rho_7 & \rho_7 & -\rho_8 - d_8 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & \rho_8 & -d_9 \end{pmatrix} \begin{pmatrix} C_{i,j,1}^{n,m} \\ C_{i,j,2}^{n,m} \\ C_{i,j,3}^{n,m} \\ C_{i,j,4}^{n,m} \\ C_{i,j,5}^{n,m} \\ C_{i,j,6}^{n,m} \\ C_{i,j,7}^{n,m} \\ C_{i,j,8}^{n,m} \\ C_{i,j,9}^{n,m} \end{pmatrix}$$

Infection terms

The forces of infection below are concerned with acquiring infection. The terms are of the form

$$FOI_{i,j,k}^{n,m} = \lambda_{i,j,k}^{n,m} S_{i,j,k}^{n,m}$$

where $\lambda_{i,j,k}^{n,m}$ is the force of infection for the subcategory in question. Relative risks of HCV transmission for recent injectors, non-recent injectors, high risk injectors, those on OST or NSP or both are $X_1, X_2, \Xi, \Gamma, \Pi$ and B respectively. The spontaneous clearance rate of HCV is δ and the base transmission rate is π. When the ordinary differential equation is for susceptible the FOI term is subtracted and the same term is added to the matching infectious category.

$$\lambda_{0,0,k}^{1,l} = \pi \mathrm{X}_1 (1-\delta)\Upsilon$$
$$\lambda_{0,0,k}^{2,l} = \pi X_2 (1-\delta)\Upsilon$$

$$\lambda_{0,0,k}^{3,l} = \pi (1-\delta)\Upsilon$$
$$\lambda_{0,0,k}^{1,h} = \pi \mathrm{X}_1 \Xi (1-\delta)\Upsilon$$
$$\lambda_{0,0,k}^{2,h} = \pi X_2 \Xi (1-\delta)\Upsilon$$

$$\lambda_{0,0,k}^{3,h} = \pi \Xi (1-\delta)\Upsilon$$
$$\lambda_{0,1,k}^{n,m} = \Gamma \lambda_{0,0,k}^{n,m}$$
$$\lambda_{1,0,k}^{n,m} = \Pi \lambda_{0,0,k}^{n,m}$$
$$\lambda_{1,1,k}^{n,m} = \mathrm{B} \lambda_{0,0,k}^{n,m}$$

Define

$$C^{n,m} = \sum_{k=1}^{9} \left(C_{0,0,k}^{n,m} \quad C_{0,1,k}^{n,m} \quad C_{1,0,k}^{n,m} \quad C_{1,1,k}^{n,m} \right),$$

$$S^{n,m} = \sum_{k=1}^{9} \left(S_{0,0,k}^{n,m} \quad S_{0,1,k}^{n,m} \quad S_{1,0,k}^{n,m} \quad S_{1,1,k}^{n,m} \right),$$

$$I = \begin{pmatrix} 1 \\ \Gamma \\ \Pi \\ \mathrm{B} \end{pmatrix},$$

to give

$$\Upsilon = \frac{\left(\mathrm{X}_1 (C^{1,l} + \Xi C^{1,h}) + X_2 \left(C^{2,l} + \Xi C^{2,h}\right) + (C^{3,l} + \Xi C^{3,h})\right) I}{\left(\mathrm{X}_1 \left(C^{1,l} + S^{1,l} + \Xi (C^{1,h} + S^{1,h})\right) + X_2 \left(C^{2,l} + S^{2,l} + \Xi (C^{2,h} + S^{2,h})\right) + (C^{3,l} + S^{3,l} + \Xi (C^{3,h} + S^{3,h}))\right) I}$$

Treatments

There are a fixed number of treatments per year, given by Φ. When the total number of infected individuals in the model is greater than this number, the treatments are allocated proportionately. When the total number of infected individuals is less than the number of possible treatments per year, all are treated. Only the first two disease progression categories are eligible for treatment and

will have treatment terms. If the ordinary differential equation is for an infected category the treatment term will be subtracted and for a susceptible category the term will be added.

If

$$\Phi < \sum_{k=1}^{5}\sum_{n}^{3}\sum_{m,i,j} C_{i,j,k}^{n,m} = C^{treat},$$

$$T_{i,j,k}^{n,m}\left(C_{i,j,k}^{n,m}\right) = \frac{\alpha\Phi C_{i,j,k}^{n,m}}{C^{treat}},$$

for $k = 1,2 \dots 5, n = 1,2,3.$

Otherwise

$$T_{i,j,k}^{n,m}\left(C_{i,j,k}^{n,m}\right) = \alpha C_{i,j,k}^{n,m},$$

for $k = 1,2 \dots 5, n = 1,2,3.$

For ex-PWID treatment is more straightforward with a proportion, r of the chronically infected and compensated cirrhosis individuals being treated each year.

$$T_k^4\left(C_k^4\right) = \alpha r C_k^4,$$

for $k = 1,2 \dots 5$

As an example here is the ordinary differential equation for the susceptible category for the first disease progression category, no interventions, recent injector (<3 years) and low risk. On the right hand side in order from left to right there is an inflow term, injecting duration terms, intervention terms, high/low risk terms, disease progression terms, infection term and treatment term.

$$\frac{dS_{0,0,1}^{1,l}}{dt} = \theta(1-\phi) + ID_{0,0,1}^{1,l} + IT_{0,0,1}^{1,l} + HR_{0,0,1}^{1,l} + DS_{0,0,1}^{1,l} - \lambda_{0,0,1}^{1,l} S_{0,0,1}^{1,l} + T_{0,0,1}^{1,l}$$

MODEL PARAMETERS

TABLE S2 MODEL PARAMETERS

Parameter	Symbol	Value/Range	Reference
Epidemiological and Demographic parameters			
Number of new injectors per year	θ	Fitted to obtain population sizes	Bristol (21, 22), Walsall (22) and unpublished estimates, Dundee adjusted from (23). See Table S2 and supporting information
Combined death and cessation rates per year	μ_i	Fitted to obtain injecting duration profiles for each setting	Lower bounds of 0.004 and 0.008 were chosen to ensure the leaving rate was greater than the likely death rate (24). See Table S2 and supporting information
Infection rate per year	π	Fitted to obtain HCV prevalence required in each setting	See Table S2 and supporting information
Proportion of new infections which spontaneously clear	δ	Sampled from uniform distribution (0.22-0.29)	(15)
Leaving rate per year from high to low risk behaviour	ζ	Sampled range (0.6761-1.617)	Data from cohort study (12) found 78/145 injectors no longer homeless after 8 months. Transition probability sampled

			from beta distribution α= 78 and $\beta = 67$ and converted to instantaneous rate
Recruitment rate per year from low risk to high risk behaviour	σ	Fitted to obtain required high risk proportions in each setting	See Table S2 and supporting information
Intervention Related parameters			
Leaving rate per year off OST	γ	1-3	Duration on OST was 8 months (4-12 months) in cohort of PWID in UK (24)
Leaving rate per year off HCNSP	κ	0.37-0.77	Welsh cohort study 61% PWID still >100% NSP after 1 year. Duration on NSP was 1.3-2.7 years. (25)
Recruitment rate per year on to OST	β	Fitted to obtain required OST coverage proportions in each setting	See Table S2 and supporting information
Recruitment rate per year on to HCNSP	η	Fitted to obtain required high NSP coverage proportions in each setting	See Table S2 and supporting information
Proportion of treatments achieving SVR prior to 2015	α	Sampled from uniform distribution (0.3992-0.6653)	Weighted mean of pooled intention to treat SVR for genotypes 1 and 2/3 taken from treatment data for PWID in UK (26)
Proportion of treatments achieving SVR post 2015	α	Sampled from uniform distribution (0.859-0.915)	(27)Weighted mean of SVR for genotype 1 (90%) and genotypes 2/3 (82-93%) from (28).
Number of PWID's treated per year	Φ	Bristol – 18 Dundee – 34 (2009 to 2015), and then 40 (2015 onwards) Walsall – 2	Number of HCV treatments in 2011. Assumed treatment of PWIDs commenced in 2009(26). More recent estimate for Dundee (personal communication John Dillon). Walsall value assumed same rate per infected PWIDs as Bristol.
Relative Transmission Risk parameters			
Risk associated with being on OST only	Γ	0.41(0.22-0.75) sampled from Lognormal distribution	Odds ratio and 95% CI from pooled analysis (in press NIHR report)
Risk associated with being on HCNSP only	Π	0.59(0.36-0.96) sampled from Lognormal distribution	Odds ratio and 95% CI from pooled analysis (in press NIHR report)
Risk associated with being on both OST and HCNSP	$\Gamma \times \Pi$	0.26 (0.09-0.64)	Calculated as product of risk associated with being solely on OST or NSP. Compares well to estimate from systematic review 0.29 (0.13-0.65) (in press NIHR report)
Risk associated with being a recent injector compared to a long-term injector*	X_1	1.53(0.93-2.52) sampled from Lognormal distribution	Odds ratio from pooled analysis (in press NIHR report)
Risk associated with being in the high risk category	Ξ	Scotland: 2.13(1.40-3.24) Bristol and Walsall: 2.75(1.97-4.22). Both sampled from lognormal distribution	Odds ratio from pooled analysis. For Scotland, the OR is just for homelessness because there is little crack injection, whereas it is for crack injection or homelessness for Bristol and Walsall

Parameter description	symbol	Distribution	Source
Yearly progression rate from f0 to f1	ρ_1	0.529-0.2095 sampled from normal distribution	PWID specific instantaneous rates from (29)
Yearly progression rate from f1 to f2	ρ_2	0.0216-0.1013 sampled from normal distribution	
Yearly progression rate from f2 to f3	ρ_3	0.0450-0.1145 sampled from normal distribution	

Yearly progression rate from f3 to compensated cirrhosis	ρ_4	0.0513-0.1838 sampled from normal distribution	
Yearly progression rate from compensated cirrhosis to decompensated cirrhosis	ρ_5	0.0166-0.0921	Instantaneous rates calculated from sampled beta distributions of transition probabilities in (16)
Yearly progression rate from compensated cirrhosis or decompensated cirrhosis to hepatocellular carcinoma	ρ_6	0.0003-0.0684	
Yearly progression rate from decompensated cirrhosis or HCC to liver transplant	ρ_7	0.0062-0.0962	
Yearly progression rate from liver transplant to post liver transplant	ρ_8	1.0423-2.4412	
Decompensated cirrhosis related death rate per year	d_6	0.1063-0.1842	
Hepatocellular carcinoma related death rate per year	d_7	0.3904-0.7697	
Liver transplant related death rate per year	d_8	0.0911-0.4348	
Post liver transplant related death rate per year	d_6	0.0280-0.1016	
Relative risk for progression rate from compensated to decompensated cirrhosis (ρ_5) following SVR	e_5	0.07 (95%CI 0.03,0.2)	Sampled from transformed lognormal distribution (19)
Relative risk for progression rate from compensated cirrhosis to HCC (ρ_6) following SVR	e_6	0.23 (95%CI 0.16,0.35)	Sampled from transformed lognormal distribution (18)

MODEL CALIBRATION

Model calibration was carried out in three steps with 1000 parameter sets obtained at each step:

1. Population size and injecting duration fitting using a PWID demographic sub-model without infection.
2. NSP and OST coverage fitting using a sub-model that includes HCV transmission but no disease progression.
3. HCV prevalence fitting using the full model with disease progression.

Step 1

In Dundee, survey data (30) suggested that the proportion of the PWID population in each injecting duration category was stable from 2008 to 2014, and so we assumed a constant population size estimated from unpublished data from Scotland. In Bristol and Walsall, size estimation data suggests that the PWID population has decreased by between 10% and 30% between 2009 and 2011 (21, 22, 31, 32). Concurrently, survey data(14, 30, 33-35) suggests the proportion of PWID injecting for longer than 10 years has increased whilst the proportion injecting for between 3 and 10 years decreased as shown in Figure 4.2a and 4.2b. There has been little change in the proportion injecting for less than 3 years. It was assumed that these changes were partly due to a decrease in the initiation rate of new injectors and a change in the cessation rates of non-recent and long-term injectors. We allowed for uncertainty around these parameters and estimated them by fitting the model to the population size and injecting duration profile (proportion of PWID in each injecting duration category) at two points in time for Walsall and Bristol and one time point for Dundee. This fitting was done with a demographic sub-model, which only had three injecting duration categories and no other stratification. We assumed that the PWID population size was at equilibrium initially (before 2004, 2006 and 2008 for Bristol, Walsall and Dundee, respectively). We sampled 1000 values for this 'stable' initial population size and the cessation rate from the recent injector category for each setting. For each of these 1000 parameter sets, the wide prior distributions for the cessation rates from non-recent and long-term injectors (see Supplementary Table 2) were then sampled, and for each sample the model was fit to the initial population size by calculating a suitable PWID recruitment rate using the steady state equations for the demographic sub-model (more details in Appendix 1). Parameter sets were retained if the resulting injecting duration profile lay within the ranges suggested from data, otherwise the cessation rates were resampled. We then sampled 1000 estimates for the later population size in 2011 for Bristol and Walsall, as well as new cessation rates for non-recent and long-term injectors, and the PWID recruitment rate was re-calibrated to fit to this new sampled population size for the 2011 data (only Bristol and Walsall). This refitting of the demographic sub-model was done using the Matlab algorithm fzero applied to the analytic solution of the model with initial conditions from the first step of fitting. Parameter sets were retained if the resulting injecting duration profile lay within ranges suggested from data for years 2004 and 2011 for Bristol and 2008 and 2011 for Walsall, otherwise the new cessation rates for this second step were resampled to obtain a fit to each of the first step parameter sets (1000 each for Bristol and Walsall).

Step 2

Coverage levels for PWID currently on OST have increased over the last 12 years. In Bristol, the proportion of PWID currently on OST increased from 40% in 2004 (33) up to 81% in 2009(14). In Walsall, OST coverage increased from 40% in 2006 to 70% in 2009 (36), and in Dundee it increased from 43% in 2008 to 72% in 2014 (37). Conversely, over this same time period, the proportion of PWID with >100% NSP coverage remained stable in both Bristol (55%) (14, 30, 33) and Walsall (38%) (30), while it increased over time in Dundee from 41% in 2008 to 60% in 2014(30). Modelled OST coverage levels for each city were calibrated to this coverage data by varying the recruitment rate onto each intervention. A service provision estimate of NSP coverage was calculated for each setting using data on needles distributed from the costings analysis (2014 data), population size (calculated from the model in 2014) and injecting frequency from survey data. Bootstrap samples of the mean injecting frequency were calculated for each setting using UAM (Bristol and Walsall) and NESI (Dundee) data. In addition the mean injecting frequency in Dundee has decreased from 717 injections per year in 2008 to 388 injections per year in 2014. Therefore an estimate of NSP coverage was calculated for each time point. The average service provision estimates of NSP coverage were 56% and 28% in Bristol and Walsall respectively in 2014 and 27% and 49% in 2008 and 2014 respectively for Dundee (see Supplementary Table 2 for more details). The recruitment rates were estimated using an intervention sub-model that incorporated no onward disease progression as these mechanisms have little effect on the coverage levels obtained. Using the Matlab fitting algorithm lsqnonlin, recruitment rates were found to fit the sub-model to the initial and endpoint coverage of each intervention as shown in Supplementary Table 2, while assuming coverage levels were quasi stable. In the full model, the recruitment rates for the initial coverage level was first used to obtain initial conditions for the first time point for each city, and then the recruitment rate was gradually varied linearly between the two values to obtain the required increase in coverage for that city.

Survey data suggests that the prevalence of crack injecting and/or homelessness, our markers of high HCV transmission risk, have remained stable in Dundee (33% homeless) and Walsall (52% homeless or crack injection), whereas it has increased in Bristol from 75% in 2004 to 87% in 2014 (homeless or crack injection). We assumed that a proportion of injectors are high-risk when they initiate injecting, which is consistent with available data(12). The leaving rate from these high-risk categories was estimated from a cohort study on homelessness which found that approximately two thirds of homeless PWID are no longer homeless after one year(12). This agrees with unpublished findings from a Welsh cohort study for both crack and homelessness(11, 25). The leaving rate was sampled 1000 times and used for all three setting. The proportion of PWID that are high-risk was also sampled 1000 times for each setting. The recruitment rates were then calculated for each parameter set using the steady state solution of the high/low risk sub-model (two variables). In Bristol, where the proportion of PWID that are high-risk has increased, we calculated a second recruitment rate for the second time point (2014) using the same method. For Bristol, the recruitment rate was gradually varied linearly to obtain the increase in the proportion of PWID that are high-risk.

Step 3

The last step of the model calibration involved fitting the full model to the HCV prevalence data from each setting (sampled 1000 times from the ranges given in Supplementary Table 2). This incorporated the 1000 parameter sets from the previous model calibration steps, and involved

calibrating the model's infection rate using the lsqnonlin function in Matlab. The model was first fit to the initial prevalence estimate (sampled from the ranges given in Supplementary Table 2) in 2004, 2006 and 2008 for Bristol, Walsall and Dundee, respectively (Supplementary Figure 1 and Supplementary Table 2), while assuming the epidemic was in a stable state at that time. For Walsall and Bristol, this one infection rate well captured the subsequent baseline epidemic dynamics (slightly increasing in Bristol and Walsall) and so no change in the infection rate was assumed after that point. The baseline transmission rates in Bristol and Walsall were comparable (0.07-0.21 and 0.09-0.22 respectively), whereas Dundee had a slightly higher baseline transmission risk (0.16-0.39. However, for Dundee we needed to fit a second increased infection rate (0.36-0.94) to capture the increase in HCV prevalence from 2008 to 2014 (using the parameters from the first prevalence fitting step as the initial conditions). This either suggests the epidemic was not stable in 2008 or that there has been a change in the risk profile of PWID in Dundee that is not fully captured by changes in intervention coverage or the prevalence of high-risk behaviours. Supplementary Table 2 and Supplementary Figure 1 show the model parameters that were fitted in the model.

TABLE S3 SUMMARY OF DATA COLLATED FOR EACH SETTING FOR MODEL CALIBRATION

	Bristol	Walsall	Dundee	Relevant parameter
Current PWID population size	**2004**: sampled 111-125% (22) of 2011 value(21). **2011**: 2025-2564 adjusted from(21) to include only 60% of people on OST not in contact with other services (21). Sampled uniformly	**2006**: 125%(22) of 2011 value **2011**: 1296-1623 estimated from local number on OST and unpublished PWID prevalence estimates for West Midlands. Sampled uniformly	Constant level 675-825 local estimate adjusted from (23) Sampled uniformly	θ, Number of new injectors per year Value of θ found using steady state equations of population sub-model for the first time point in all 3 settings. In Bristol and Walsall a second value of θ is found using Matlab fzero and analytical solution to population sub-model that gives population size required with sampled cessation rates
Injecting duration profile: Proportion of PWID that are recent (R), non-recent (NR), or long-term injectors (LT)	**2004**: R: 0.04-0.2 NR: 0.25-0.45 LT: 0.4-0.65 (UAM) **2014**: R: 0.075-0.2 NR: 0.05-0.22 LT: 0.55-0.85 (UAM)	**2006:** R: 0.1-0.3 NR: 0.45-0.65 LT: 0.2-0.3 **2014**: R:0.1-0.3 NR: 0.15-0.4 LT: 0.4-0.6 (UAM)	Constant level R: 0.15-0.35 NR: 0.36-0.65 LT: 0.12-0.35 (NESI)	Death and cessation rates (μ_i) per year. Prior distribution for μ_1 (0.0351 – 0.1702) calculated from assumption that between 10% and 40% of recent initiates cease injecting within 3 years (7). A large upper bound of 0.4 was assumed for the prior distributions of μ_2 and μ_3 due to lack of information. Lower bounds of 0.004 and 0.008 were chosen to ensure the leaving rate was greater than the likely death rate (24) Parameter sets accepted if PWID demographic sub-model fits were within the ranges for each injecting duration
Chronic HCV Prevalence (75% of HCV Ab prevalence)	Constant level 40-50% (community surveys, UAM) Sampled from truncated Beta(305.25,364.75)	**2006**: 11-26% (UAM) Sampled from truncated Beta(30.75,132.25) **2014**:	**2008**: 15-30% (NESI) Sampled from truncated Beta(18.75,64.25) **2014**:	π, infection rate used to fit the HCV prevalence estimates

		15-39% (no fitting required)	19-32% adjusted from (NESI) Sampled from truncated Beta(43.45,125.55)*	
Proportion high risk	**2004:** 70-80% (2004, 2006 community surveys and UAM). Sampled uniformly. **2014:** 80-95% (UAM). Sampled uniformly.	Constant level of 40-65% (UAM). Sampled uniformly.	Constant level of 26-42% (NESI). Sampled from Beta (156,315).	ϕ, proportion of injectors initially high risk assumed same as sampled proportion high risk σ, recruitment rate per year from low to high risk behaviour, calculated from sampled leaving rate ζ and proportion high risk ϕ.
Proportion on OST	**2004**: 33.3-46.7% (38) sampled from truncated Beta(81,121) **2009**: 76.5-86.3% (community survey, 2009) sampled from truncated Beta(241,55)	**2006**: 30-50% (UAM) sampled from truncated Beta(32,48) **2009**: 61-82% (UAM) sampled from truncated Beta(47,18)	**2008**: 433-53% (NESI) sampled from Beta(36,47) **2014**: 65-79% (NESI) sampled from Beta(106,40)	β, recruitment rate per year onto OST
Proportion >100% NSP (needles distributed /(population size*injecting frequency))	Needles distributed in 2014 (786542-844646), population size in 2014 and injecting frequency (470-859 per year from UAM) sampled. Mean calculated coverage 56%	Needles distributed in 2014 (225275-237111), population size in 2014 and injecting frequency (435-716 per year from UAM) sampled. Mean calculated coverage 28%	Needles distributed in 2014 (assumed same in 2008), population size in 2008 and injecting frequency (517-999 per year from NESI) sampled. Mean calculated coverage 27%. Needles distributed in 2014 (138246-145768), population size in 2014 and injecting frequency (251-533 per year from NESI) sampled. Mean calculated coverage 49%	η, recruitment rate per year onto high coverage NSP

- *Chronic prevalence was available from the NESI survey for 2014

SUB-MODELS USED IN THE FITTING PROCEDURE

Injecting duration model

A model with 3 injecting duration categories was used to fit the population data and the injecting duration profiles from survey data. Here S^i is the number of susceptible injectors in the i category. The categories are: r, recent injector, n, non-recent injector and l, long-term injector. The μ_i and τ_i are the same as the full model.

$$\frac{dS^r}{dt} = \theta - (\mu_1 + \tau_1)S^r$$

$$\frac{dS^n}{dt} = \mu_1 S^r - (\mu_2 + \tau_2)S^n$$

$$\frac{dS^l}{dt} = \mu_2 S^n - \mu_3 S^l$$

The steady state solution of this model is given below:

$$S^r = \frac{\theta}{\mu_1+\tau_1}, S^n = \frac{\theta\tau_1}{(\mu_1+\tau_1)(\mu_2+\tau_2)}, S^l = \frac{\theta\tau_1\tau_2}{(\mu_3(\mu_1+\tau_1)(\mu_2+\tau_2))},$$

with total population $N = S^r + S^n + S^l$.

The analytical solution of this system is

$$S^r(t) = S^r(0)e^{-(\mu_1+\tau_1)t} + \frac{\theta}{\mu_1+\tau_1}\left(1 - e^{-(\mu_1+\tau_1)t}\right),$$

$$S^n(t) = \frac{\tau_1\theta}{(\mu_1+\tau_1)(\mu_2+\tau_2)} + S^n(0)e^{-(\mu_2+\tau_2)t} + \frac{\tau_1}{\mu_1+\tau_1-\mu_2-\tau_2}S^r(0)(e^{-(\mu_2+\tau_2)t} - e^{-(\mu_1+\tau_1)t})$$
$$+ \frac{\tau_1\theta}{\mu_1+\tau_1-\mu_2-\tau_2} * \left(e^{-(\mu_1+\tau_1)t}/(\mu_1+\tau_1) - e^{-(\mu_2+\tau_2)t}/(\mu_2+\tau_2)\right),$$

$$S^l(t) = e^{-\mu_3 t}\left(S^l(0) + \frac{\tau_2}{\mu_2+\tau_2-\mu_3}.\left(\frac{\tau_1 S^r(0)}{\mu_1+\tau_1-\mu_3} - \frac{\tau_1\theta}{\mu_3(\mu_1+\tau_1-\mu_3)} + S^n(0)\right)\right)$$
$$+ \frac{e^{-(\mu_2+\tau_2)t}\tau_2}{\mu_2+\tau_2-\mu_3}\left(\frac{\tau_1 S^r(0)}{\mu_2-\tau_2+\mu_1+\tau_1} + \frac{\tau_1\theta}{(\mu_2+\tau_2)(-\mu_2-\tau_2+\mu_1+\tau_1)} - S^n(0)\right)$$
$$+ \frac{e^{-(\mu_1+\tau_1)t}\tau_1\tau_2\theta}{(\mu_1+\tau_1)(\mu_1+\tau_1-mu_3)(\mu_1+\tau_1-\mu_2-\tau_2)} + \frac{\tau_1\tau_2\theta}{\mu_3(\mu_1+\tau_1)(\mu_2+\tau_2)}$$

<u>High risk model</u>

A model with a high risk and low risk only was used to calculate parameter values in the calibration process. The variable S^h denotes high risk and S^l denotes low risk.

$$\frac{dS^h}{dt} = -\zeta S^h + \sigma S^l$$
$$\frac{dS^l}{dt} = \zeta S^h - \sigma S^l$$

As this is a closed system we have: $N - S^h = S^l$, which gives

$$\frac{dS^h}{dt} = -\zeta S^h + \sigma(N - S^h)$$

Setting the left hand side to zero and solving gives to obtain the proportion of the total population that are high risk

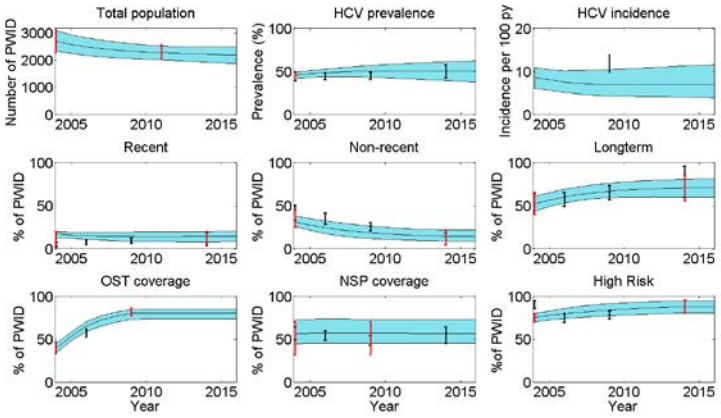
$$\Phi = \frac{\sigma}{\sigma+\zeta}$$

This expression was used to calculate the required value of the recruitment rate σ, from the sampled values of the proportion of high risk individuals and the leaving rate ζ.

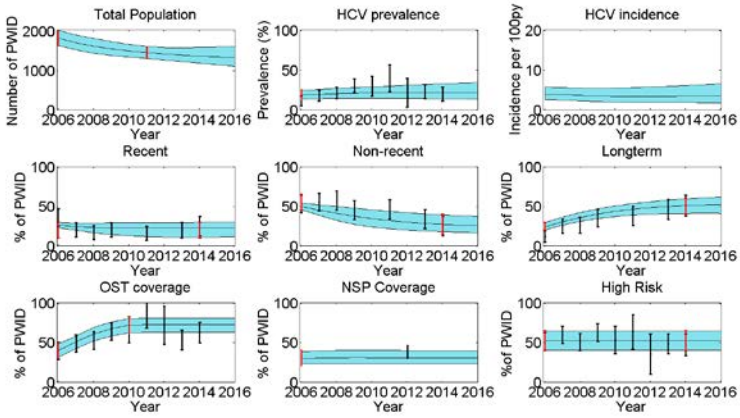
FIGURE S1 GRAPHS SHOWING FITTING OF THE BASELINE SCENARIOS IN EACH SETTING.

Error bars in black are data points from surveys, error bars in red are the ranges used for model calibration.

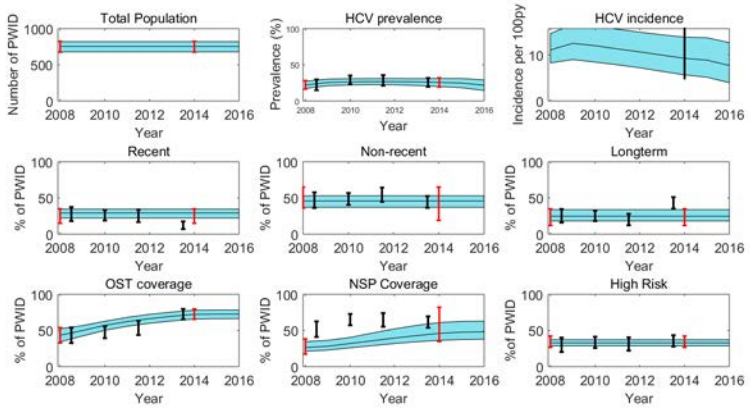
Bristol



Walsall



Dundee



Model Parametrization and Calibration

In order to capture costing uncertainty within the cost-effectiveness model, we conducted a multivariate simulation of all parameters included in the costing sensitivity analysis (described above), with uniform distribution between the minimum and the maximum values observed over 1000 iterations. The results from these 1000 iterations were fed in as the cost estimates for NSPs in the cost-effectiveness model.

Other health-related costs and QALY weights as derived from the literature were input into the model using appropriate distributions, as described in Table S1. Cost parameters were largely varied with a Gamma distribution, with the exception of treatment costs for sofosbuvir and ledipasvir; these were kept as a constant because of lack of data for a distribution. QALY weights were varied using a Beta distribution.

Results

TABLE S2 DETAILED COSTING RESULTS

	Total Needles	Total Cost	Non-IPED PWID population size	Visits per user	Cost per non-IPED PWID	Needles per non-IPED PWID
Bristol	883,524	£232,116.78	1,847-2,595	13-18	£89.45-£125.67	340-478
Dundee	150,790	£104,495.75	675-825	17-20	£126.66-£154.81	183-223
Walsall	245,002	£98,649.03	1,144-1,646	12-17	£59.93-£86.23	149-214

TABLE S3 TOTAL COSTS AND NEEDLES FOR DISTRIBUTION TO OPIATE USERS, BY CITY

	Total Needles
Bristol	
Fixed Site	
Pharmacies (n = 25)	
Other	
Total City-Wide	
Dundee	
Fixed Site	
Pharmacies (n = 5)	
Other	
Total City-Wide	
Walsall	
Fixed Site	
Pharmacies (n = 12)	
Other	
Total City-Wide	

FIGURE S2 COSTING SENSITIVITY ANALYSIS

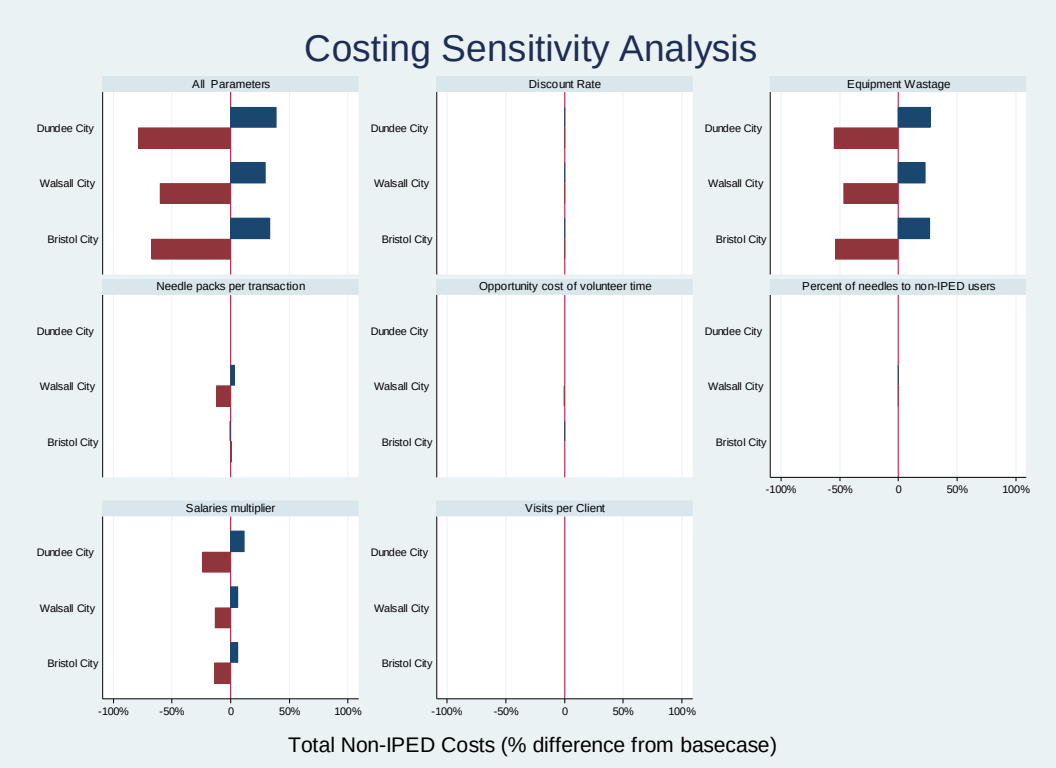


TABLE S4 TOTAL DEATHS AND INFECTIONS AVERTED THOUGH NSP OVER 50 YEARS BY CITY

	Deaths Averted			Infections Averted		
	Median	**2.5% CrI**	**97.5% CrI**	**Median**	**2.5% CrI**	**97.5% CrI**
Bristol	20.5	4.3	51.1	199.5	42.5	505.2
Dundee	2.1	0.2	24.4	84	12	663
Walsall	5.8	1.2	14.9	92.7	22.3	200.5

CrI – credible interval

Table S7 Projected total health-related costs over 50 years (GBP millions), by city

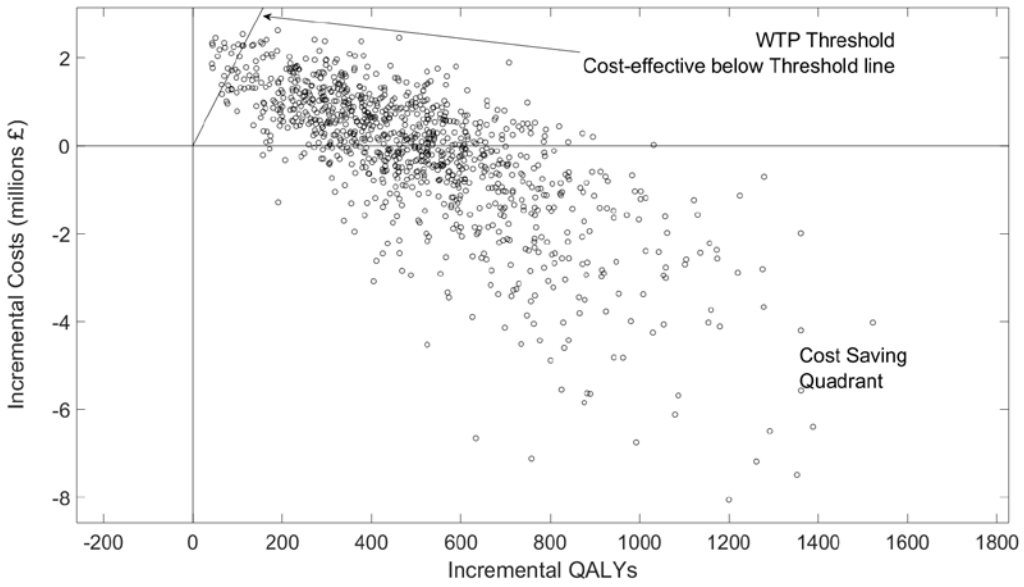
	Projected total health-related costs over 50-year time horizon (GBP millions)						
	With NSP			**No NSP for 10 years**			
Costs (2014 GBP)	**Mean**	**2.5% CrI**	**97.5% CrI**	**Mean**	**2.5% CrI**	**97.5% CrI**	**Mean Difference**
Bristol							
Healthcare[a]	£130.4	£60.0	£288.4	£131.6	£60.8	£290.1	-£1.20
HCV treatment[b] (no injecting)	£39.9	£23.9	£58.2	£41.1	£24.8	£60.1	-£1.20
HCV treatment (PWID)	£15.5	£13.6	£16.1	£15.5	£14.1	£16.1	-£0.05
NSP	£6.0	£3.7	£8.3	£3.8	£2.3	£5.3	£2.20

OST	£112.3	£86.8	£142.5	£112.2	£86.8	£142.4	£0.08
Total	**£304.0**			**£304.1**			**-£0.16**
Dundee							
Healthcare[a]	£32.2	£16.4	£68.0	£32.6	£16.7	£69.2	-£0.40
HCV treatment[b] (no injecting)	£11.4	£7.2	£16.4	£12.0	£7.5	£17.9	-£0.60
HCV treatment (PWID)	£8.8	£5.2	£14.1	£11.4	£5.6	£21.7	-£2.50
NSP	£2.9	£1.6	£4.4	£1.9	£1.0	£2.8	£1.00
OST	£37.1	£32.1	£42.3	£37.1	£32.1	£42.3	£0.0003
Total	**£92.5**			**£95.0**			**-£2.50**
Walsall							
Healthcare[a]	£64.1	£31.2	£132.4	£64.5	£31.4	£132.9	-£0.40
HCV treatment[b] (no injecting)	£23.3	£15.1	£33.1	£23.9	£15.6	£34.0	-£0.60
HCV treatment (PWID)	£1.7	£1.6	£1.8	£1.7	£1.7	£1.8	-£0.002
NSP	£3.0	£1.6	£5.3	£1.9	£1.0	£3.5	£1.10
OST	£61.7	£38.3	£96.5	£61.7	£38.3	£96.5	£0.01
Total	**£153.8**			**£153.7**			**£0.10**

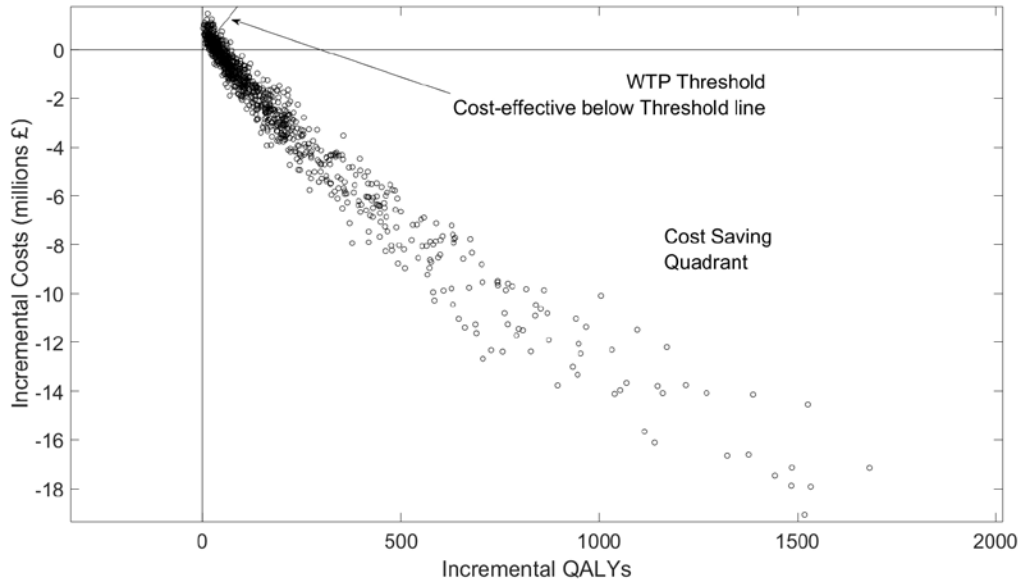
CrI – credible interval, [a]healthcare costs include costs associated with disease stage (for example liver transplantation and management of hepatocellular carcinoma), [b]HCV treatment costs include drug and staff time associated with treating HCV; NSP, Needle and syringe programmes; HCV, hepatitis C virus; OST, opioid substitution therapy; PWID, people who inject drugs.

Figure S3 Cost-effectiveness planes for each setting

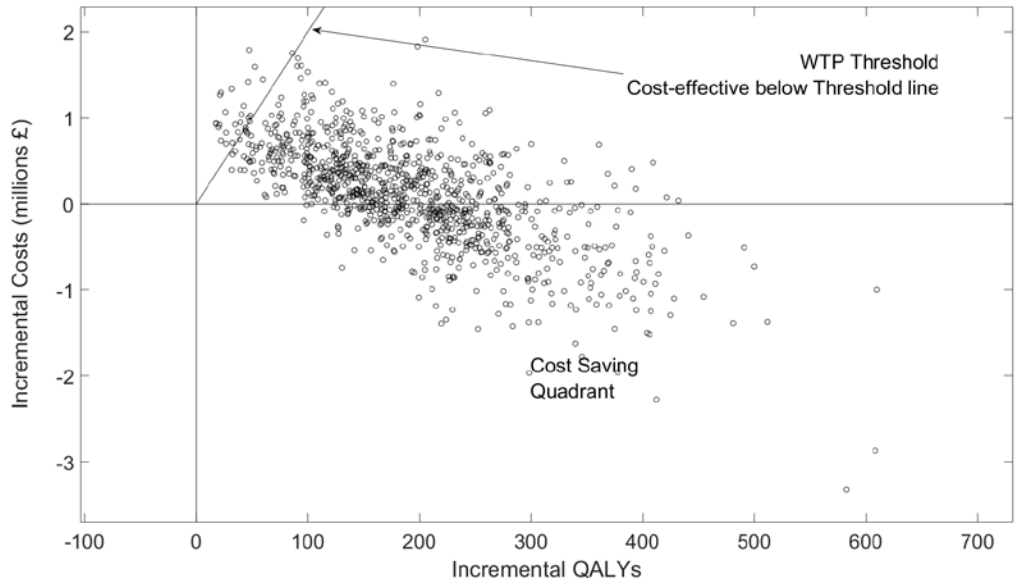
Bristol



Dundee



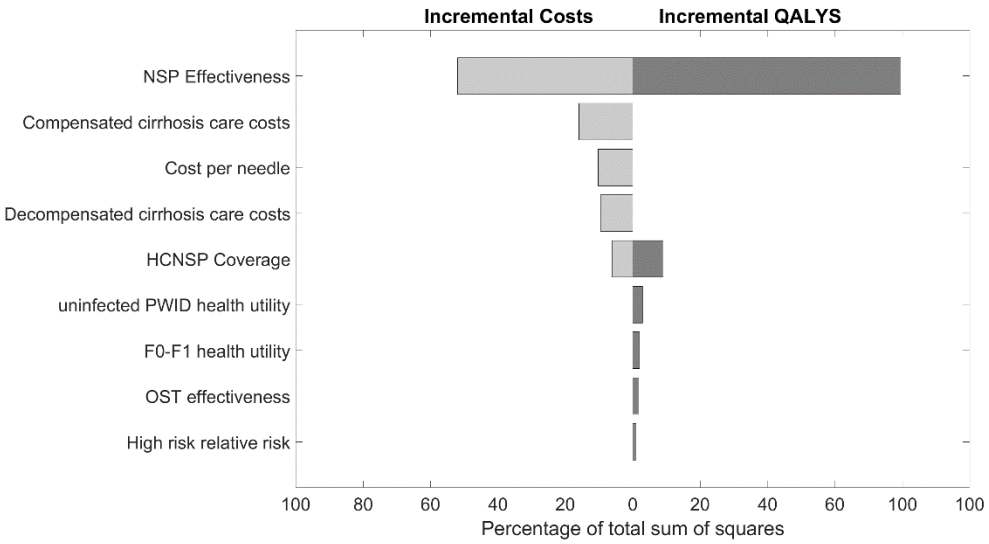
Walsall



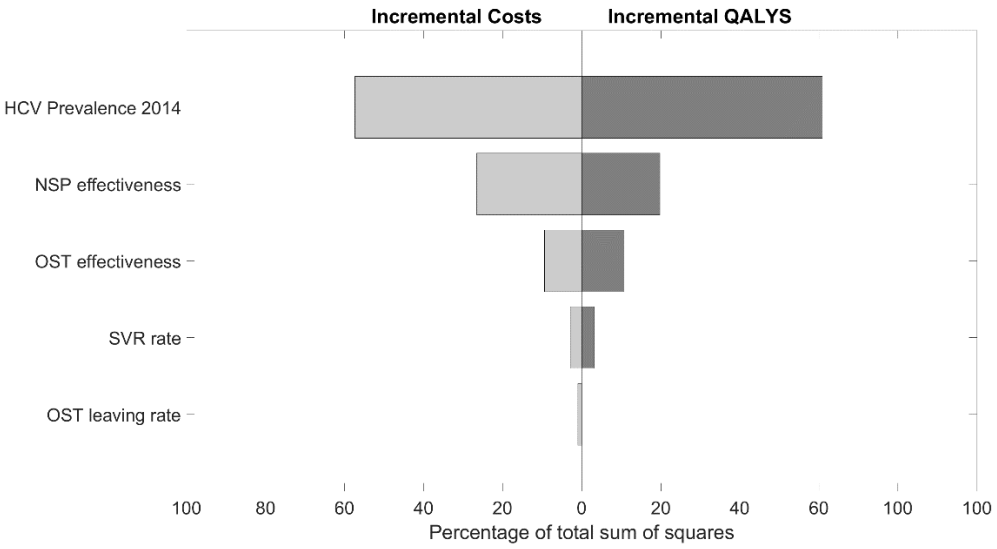
WTP, willingness to pay threshold; QALY, quality adjusted life year.

Figure S4

Bristol



Dundee



Walsall

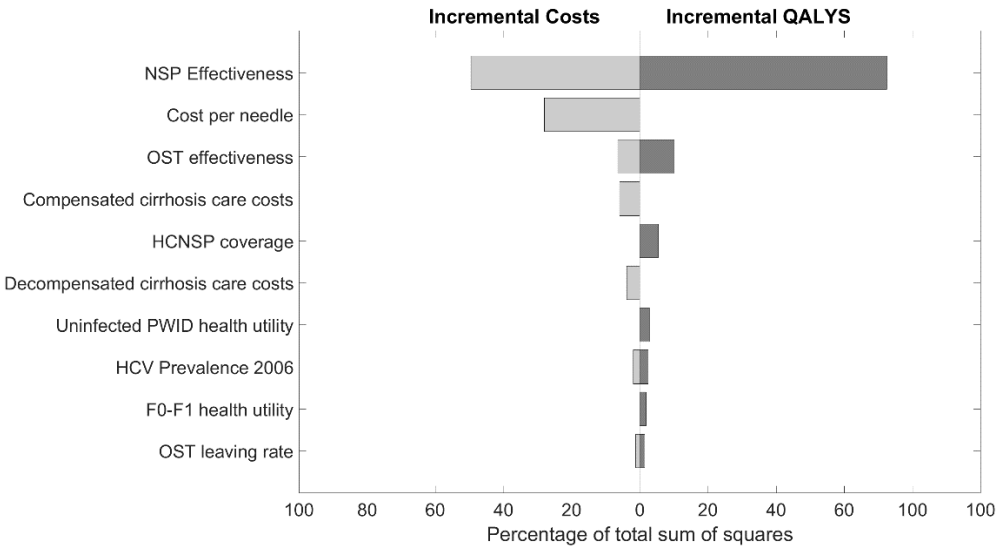
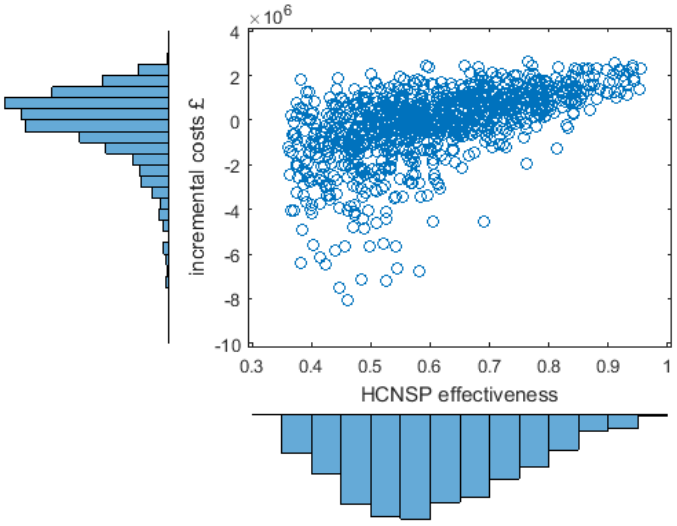
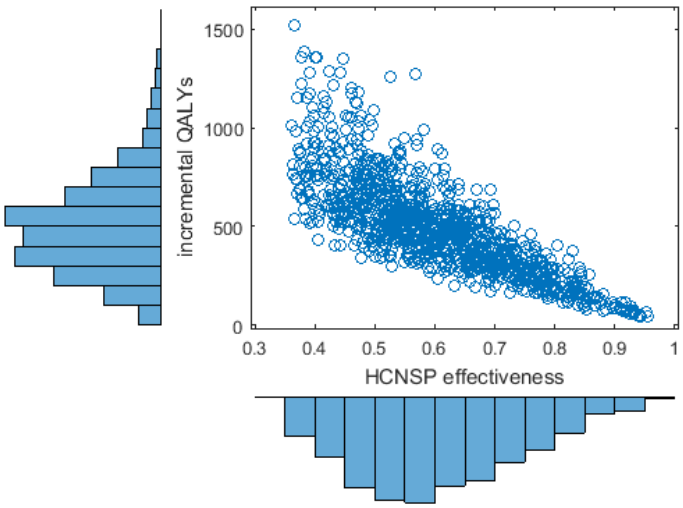


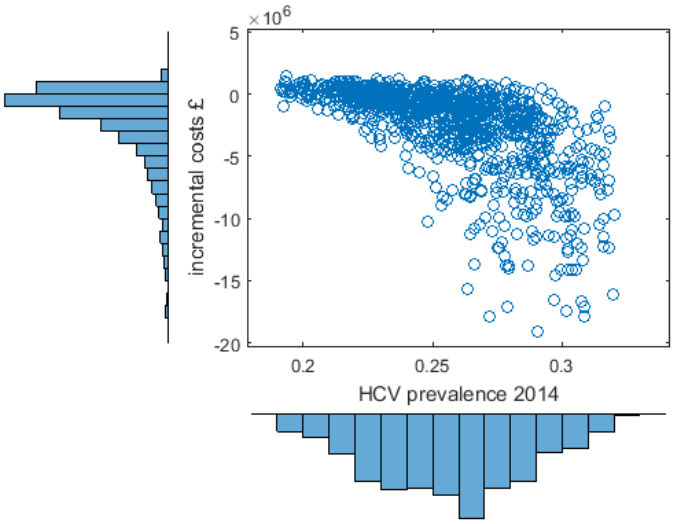
Figure S5

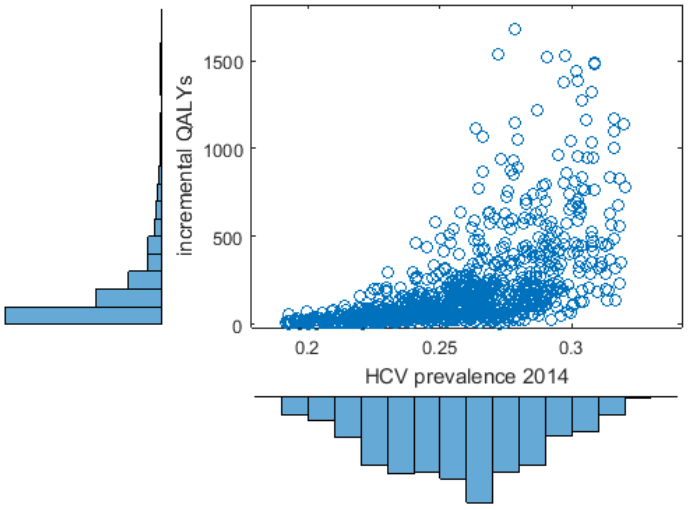
Bristol




incremental QALYs
1500
1000
500
0
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
HCNSP effectiveness

Dundee


×10^6
incremental costs £
5
0
-5
-10
-15
-20
0.2
0.25
0.3
HCV prevalence 2014


incremental QALYs
1500
1000
500
0
0.2
0.25
0.3
HCV prevalence 2014

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