**Title:** Detachable low dead space syringes for the prevention of hepatitis C among people who inject drugs in Bristol, UK: an economic evaluation

**Running title:** An economic evaluation of detachable low dead space syringes

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## Abstract

**Background and Aims:**

Traditional detachable syringes used by people who inject drugs (PWID) retain larger volumes of blood when the plunger is depressed than syringes with fixed needles - referred to as high (HDSS) and low dead space syringes (LDSS), respectively. Evidence suggests that using HDSS may result in greater hepatitis C virus (HCV) transmission risk than LDSS. We evaluated the cost-effectiveness of an intervention to introduce detachable LDSS in a needle and syringe programme (NSP).

**Design:** HCV transmission and disease progression model with cost-effectiveness analysis using a health-care perspective. Detachable LDSS are associated with increased costs (£0.01) per syringe, yearly staff training costs (£536) and an estimated decreased risk (by 47.5%) of HCV transmission compared to HDSS. The intervention was modelled for 10 years, with costs and health benefits (quality-adjusted life-years or QALYs) tracked over 50 years.

**Setting:** Bristol, UK

**Participants/Cases:** PWID attending NSP

**Intervention and comparator:** Gradual replacement of HDSS at NSP, with 8%, 58% and 95% of HDSS being replaced by detachable LDSS in 2016, 2017 and 2018, respectively. Comparator was continuing use of HDSS.

**Measurements:** Net monetary benefit. Benefits were measured in QALYs.

**Findings:** Introducing detachable LDSS was associated with a small increase in intervention costs (£21,717) compared to not introducing detachable LDSS, but considerable savings in HCV-related treatment and care costs (£4,138,118). Overall cost savings were £4,116,401 over 50 years and QALY gains were 1,000, with an estimated 30% reduction in new infections over the 10 year intervention period. In all sensitivity analyses, detachable LDSS resulted in cost savings and additional QALYs. Threshold analyses suggested detachable LDSS would need to reduce HCV transmission risk of HDSS by 0.26% to be cost-saving and 0.04% to be cost-effective.

**Conclusions:** Replacing HDSS with detachable LDSS in NSPs is likely to be a cost-saving approach for reducing HCV transmission.

## Introduction

Hepatitis C virus (HCV) is a blood borne virus (BBV) with considerable burden globally, with over half of the estimated 15 million people who inject drugs (PWID) being infected(1). In the United Kingdom (UK), there are approximately 200,000 individuals that have been infected with HCV, of whom over 80% are PWID or have an injecting history(2,3). Hospital admissions due to end-stage liver disease and hepatocellular carcinoma (HCC) nearly tripled between 2004 and 2013, while deaths from HCV more than doubled(4).

The primary interventions for preventing HCV transmission are needle and syringe programmes (NSP) and opioid substitution therapy (OST), which have high coverage (>50%) in the UK(5). Although evidence suggests these interventions are effective at reducing the risk of HCV acquisition(6), HCV transmission rates among PWID remain high in the UK(4) and globally(1).

PWID either use syringes with fixed or detachable needles. Syringes with fixed needles are traditionally termed low dead space syringes (LDSS) because their design minimises the amount of dead space between the syringe hub and needle (volume of space in which fluid is retained) when the plunger is fully depressed(7,8). In contrast, traditional syringes with detachable needles have greater dead space, and are termed high dead space syringes (HDSS) (Figure 1). Existing evidence suggests that if LDSS are re-used they will be less infectious than HDSS because they retain less blood(9). Laboratory studies have shown that LDSS retain less viable HCV in the syringe in subsequent injections than HDSS(8,10), while modelling(11,12) has shown that smaller quantities of blood are transferred with LDSS than HDSS. Limited epidemiological studies also suggest lower HIV and HCV prevalence rates among PWID that use LDSS(13–16), although these studies have not measured incident infection and only one UK study adequately controlled for other factors that could affect infection risk(13).

The World Health Organisation (WHO)(17) and National Institute for Health and Care Excellence (NICE)(18) recommend that NSPs provide and encourage the use of LDSS by PWID. However, most LDSS are only available in small sizes (≤1 ml) with short needles(7), and so PWID requiring or preferring larger syringes and/or detachable or longer needles typically use HDSS. To meet this need, detachable syringes or needles with reduced dead space (detachable LDSS, see Figure 1) have been developed. Studies suggest that detachable syringes with low dead space needles (second syringe in Figure 1) can retain less viable HCV and HIV than traditional detachable syringes(8,19), either with rinsing or not and before or after storage, although some differences are not statistically significant.

We introduced an intervention to support the introduction of detachable LDSS (detachable syringes with low dead space needles) in Bristol Drugs Project (BDP)(20) in April 2016, nearly replacing all detachable HDSS by 2018. Our analysis assesses the cost-effectiveness of this intervention, compared to a counterfactual scenario where the intervention was not implemented.

## Methods

### Model description

A dynamic compartmental model (Figure 2) of HCV transmission and disease progression was developed(21).

The model is open, with individuals entering due to initiation of injection drug use (IDU), and leaving due to mortality. Individuals experience a risk of infection due to their IDU, dependent on the prevalence of HCV among PWID and the degree to which PWID use different types of needle/syringe. If infected, some individuals spontaneously clear their infection and become susceptible to infection again, while the remainder develop chronic HCV infection and progress through the disease states in Figure 2. Current PWID can cease injecting whereupon they enter the ex-injector state. Susceptible individuals in this state can no longer become HCV-infected, but if already infected they continue to progress through the same HCV disease states.

All individuals experience the same background mortality rate, with current PWID also experiencing drug-related mortality(22) while those in the decompensated cirrhosis, hepatocellular carcinoma (HCC), liver transplant and post-transplant states experience liver-related mortality(23). PWID with HCC or undergoing liver transplant are assumed to not be injecting and so are not infectious.

Individuals in the mild, moderate or compensated cirrhosis states of chronic HCV infection can receive HCV treatment. Treatment involves direct-acting antivirals (DAA), which have high cure rates (sustained viral reponse [SVR] is 95%) and 12-week duration(24–27). For those who achieve SVR in the mild and moderate states, no further disease progression occurs, whereas disease progression rates are reduced by 77-78% for those who achieve SVR in the cirrhosis state(28,29); this progression continues at the same rate once they reach decompensated cirrhosis or HCC. PWID who achieve SVR can be re-infected at the same rate as for their primary infection.

The model uses a cycle length of 1 year, with half-cycle correction(30). The differential equations for the model are in the supplementary materials.

## Model parameterisation

The model was parameterised using data from surveys among PWID in Bristol and the published literature (Table 1 and 2). Cost and intervention-related data was provided by BDP.

### Transmission parameters for different syringe types

The model assumes that fixed LDSS, detachable LDSS and detachable HDSS are associated with differing HCV transmission risk. However, given the lack of direct estimates for the effectiveness of each type of syringe for reducing the risk of HCV transmission among PWID, indirect estimates of their relative infectiveness was obtained from syringe experiments undertaken by Binka et al(8). These experiments estimated the degree to which viable hepatitis C virus could be recovered from different types of the syringe following contamination with HCV-spiked plasma and their plunger fully depressed. Fixed LDSS (insulin syringes) were compared with detachable HDSS (tuberculin syringes) and two types of detachable LDSS. Here, we only consider the Nevershare detachable LDSS with low dead space needle because this was used in Bristol. In the experiments done by Binka(8), they found that fixed LDSS had the fewest syringes with detectable virus, while detachable LDSS had fewer syringes with detectable virus than detachable HDSS. The proportion detectable also depended on the gauge of the needle used (Table 3). Among syringes with detectable virus, they also found that fixed LDSS had the lowest quantity of detectable virus, with detachable LDSS having less than detachable HDSS (Table 3). This data was used to produce estimates for the relative infectivity of the different syringe types by assuming infectivity was related to the product of the proportion of syringes that have detectable virus and the amount of residual detectable virus in those syringes. Our calculations

also assumed that 46.1% of detachable needles are 23G1¼" gauge and 53.9% are 25G" gauge, based on Bristol data. In the probabilistic sensitivity analysis, we incorporated uncertainty in these estimates by sampling (10,000 times) from the uncertainty distributions for the proportion of detachable syringes that were each type of gauge (beta distribution), the proportion of each type of syringe that had detectable virus (beta distribution), and the quantity of detectable virus found in each type of syringe (gamma distribution). These calculations suggest that detachable LDSS are 47.5% (95% credibility interval or CrI 33.5-58.9%) less infectious than detachable HDSS and fixed LDSS are 73.5% (95%CrI 63.3-81.5%) less infectious, where the 95% credibility intervals are calculated as the central 95% percentile range across the different sampled estimates.

**Injecting drug use related parameters before and following the intervention**

The annual rate of sharing needles in Bristol is estimated to be 103, based on reported rates of needle sharing of 16% from Public Health England(31) and data suggesting PWID in Bristol inject approximately 646 times per year(31). Table 1 displays the distribution of syringe types used by PWID in Bristol prior to and in the years following the targeted intervention. Just considering the use of detachable syringes, this syringe distribution data shows that the intervention resulted in 8%, 58% and 95% of HDSS being replaced by detachable LDSS in 2016, 2017 and 2018, respectively. Table 2 gives the rate of drug-related death in PWID(22) and the duration until cessation of injecting(32).

**Cost and associated inputs**

The perspective adopted in the cost-effectiveness analysis was that of the National Health Service and Personal Social Services in Bristol. Considered costs included those associated with buying the syringes, implementation of the targeted intervention, HCV treatment and medical resource use.

BDP estimated that the initial implementation of the targeted intervention required one working day for two members of staff to develop and design educational posters for service users (16 hours, assuming an 8-hour work day), 45 minutes of initial training for 20 staff members on the benefits of detachable LDSS, who to offer them to, and how to encourage their use (15 hours), and 30 minutes of refresher training for 20 staff members (10 hours), totalling 41 hours of staff time.

The costs of printing educational posters was negligible given that fewer than ten posters were printed on-site. BDP confirmed that conversations with PWID on the advantages of detachable LDSS (less wasted drug and lower risk of transferring infection) would not extend the standard duration of a needle exchange conversation. However, a scenario was considered in which all needle exchange discussions were extended by 5 minutes.

The salary range for relevant staff members at BDP was £21,792-26,948, which we averaged to £24,370. Assuming standard working hours, this equates to an hourly rate of £13.07. The cost of implementing the targeted intervention was therefore £536 (=41 x £13.07), which we conservatively assumed to be incurred annually for the duration of the intervention. In the scenario where all needle exchange conversations were extended by 5 minutes, an additional cost of £595 (=546 x 1/12 x £13.07) was applied each year based on 546 needle exchange conversations taking place where HDSS were requested in the year following the introduction of detachable LDSS.

All costs were valued in 2017 UK pounds. Where necessary, costs were inflated to 2017 prices using the hospital and community health services pay and prices index from Curtis(33). Costs used in the model are presented in Table 2. BDP provided the costs of injecting equipment, with fixed LDSS costing £0.050, detachable LDSS costing £0.033 and HDSS costing £0.025. On average, 303 syringes were given

to each PWID per year. Staff training costs were obtained directly from BDP (Table 2). Based on recent data, we assume that 18 (or 2%) chronically infected PWID receive DAA HCV treatment annually in Bristol at a cost of £15,000 per treatment, with 95% achieving SVR(34). Other healthcare costs for each disease stage come from existing literature.

**Utilities and HCV progression parameters**

Utility values for each health state and the utility decrement for DAA treatment are presented in Table 2, as are the annual disease progression transition probabilities, using existing literature.

## Model calibration

In the absence of HCV treatment for PWID, the model was calibrated to give a stable population (after 50 years) of 2,770 PWID as estimated for Bristol(35), and a prevalence of chronic HCV infection of 42.5%(36). This calibration assumed midpoint estimates for all parameters, except for the annual number of individuals initiating injecting drug use and the transmission probability for sharing a HDSS, which were varied to calibrate the model, giving calibrated values of 260 and 0.40%, respectively. We refer to this calibrated model run as the **baseline model fit**. For this analysis, the baseline model fit was then run with HCV treatment available from 2009, either including the detachable LDSS intervention from 2016 (intervention scenario), or a counterfactual scenario where no detachable LDSS intervention occurred.

## Cost-effectiveness analysis

To estimate the impact and cost-effectiveness of the BDP intervention, total costs and QALYs were calculated for both the intervention scenario and the counterfactual over a 50-year time horizon: the intervention was assumed to run for 10 years with outcomes observed over the subsequent 40 years to capture prevention and morbidity benefits. As the intervention scenario was associated with reduced costs and increased QALYs, the incremental cost-effectiveness ratio (ICER; a standard representation of cost-effectiveness) could not be interpreted and so the net monetary benefit (NMB = (incremental QALYs x willingness-to-pay threshold) – incremental costs) was calculated. A willingness-to-pay threshold of £20,000 per QALY was assumed, as recommended by NICE(37). Costs and outcomes were discounted at a rate of 3.5% per annum.

## Sensitivity analysis

One-way sensitivity analysis (OWSA) and probabilistic sensitivity analysis (PSA) were performed on the impact and cost-effectiveness projections where parameters in the baseline model fit were varied. The parameter ranges used in OWSA (95% confidence intervals where available; otherwise +/- 25%) and probability distributions used in PSA are in Table 2.

Scenario analyses were also considered in which the time horizon was set to 10 years and 20 years instead of 50 years; outcomes discounted at 1.5% instead of 3.5%; the cost of implementing the targeted intervention was doubled (£1,072 Instead of £536); an additional 5 minutes was needed per needle exchange conversation; treatment costs decrease from £15,000 to £7,500 in Year 4 onwards; and the antiviral treatment rate is doubled or tripled from Year 2 onwards.

**Threshold analysis on effectiveness of detachable LDSS**

Given the uncertainty in our estimates of the relative infectivity of the different syringes, a threshold analysis was conducted to determine the required reduction in transmission risk for detachable LDSS

compared to HDSS that results in the targeted intervention either being cost-saving or cost-effective at a threshold of £20,000 per QALY. Results are also presented assuming a wide range of values for the reduction in transmission risk due to detachable LDSS compared to HDSS, from 0% to 100% in 10% increments. We do not consider the scenario where detachable LDSS may increase transmission risk compared to HDSS because it is known that this scenario would not be cost-effective.

## Results

### Cost-effectiveness results

The targeted intervention was associated with cost savings of £4,116,401 and increases in QALYs of 1,000 over the 50-year timeframe (Table 4); i.e. the intervention is cheaper and results in better health outcomes than the counterfactual of not distributing detachable LDSS. Although the targeted intervention is associated with a small increase in equipment and implementation costs, there are considerable savings in HCV treatment costs and HCV-related care costs, resulting in substantial overall savings (Table 4). Assuming a willingness-to-pay threshold of £20,000 per QALY saved, the NMB was calculated to be £24,118,699. The intervention also results in a 30% reduction in incident infections over the 10-year intervention (from 1,092 to 765 infections in the PWID population in Bristol, or 327 infections averted), which diminishes to a 10% reduction in incident infections over the 50-year time horizon (from 5,224 to 4,704, or 520 infections averted).

### Sensitivity analyses

#### *Univariate sensitivity analysis*

The 10 most influential parameters affecting the NMB of the intervention, when varied individually, are presented in Figure 3. The most influential parameter is the long-term uptake of detachable LDSS following the intervention. All parameter variations still resulted in the intervention being associated with a reduction in costs and an increase in QALYs, and so the results of the base-case analysis are considered robust.

#### *Scenario analyses*

For all considered scenarios, the intervention was cheaper and resulted in better health outcomes than not distributing detachable LDSS (Figure 4). Reduced time horizons of 10 or 20 years (instead of 50 years) were associated with reductions in NMB of 90% and 65% versus the base-case. Conversely, lower discounting of outcomes (1.5% instead of 3.5%) resulted in a substantial increase in NMB of 57%. Doubling the cost of implementing the intervention (£1,072 instead of £536) and assuming an additional 5 minutes per needle exchange concversation, resulted in negligible changes (<1%) in the NMB. Future decreases in HCV treatment costs (halved in 4 years) were associated with a small (4%) decrease in NMB, while doubling or tripling future treatment rates decreased the NMB by 3% and 6%, respectively.

#### *Threshold analysis*

In the base-case analysis, detachable LDSS were associated with a 47% reduction in transmission risk compared to HDSS (as calculated in the methods). The threshold analysis demonstrates that detachable LDSS only have to be associated with a negligible reduction in transmission risk (0.26%) in

order for the intervention to be cost-saving, with this reducing to 0.04% for the intervention to be cost-effective at a willingness-to-pay threshold of £20,000 per QALY. Results associated with different reductions in transmission risk of between 0% and 100% for detachable LDSS (versus detachable HDSS) are presented in Supplementary Table 3, showing that detachable LDSS are cost-saving except for when they are not associated with a reduction in transmission risk.

**Probabilistic sensitivity analysis**

The results of 10,000 PSA simulations were plotted on the cost-effectiveness plane (CEP) (Supplementary Figure 1) with the point estimates and 95% credility intervals for the QALYs and costs being shown in Table 5. All simulations showed the targeted intervention to be associated with overall lower costs and more QALYs compared with the counterfactual where the intervention is not implemented. The mean incremental costs over the simulated results were -£3,896,754 (95%CrI -£6,313,555 to -£2,121,271), and the mean incremental QALYs was 951 (95%CrI 455-1,635), which is relatively consistent with the base-case change in costs and QALYs of -£4,116,401 and 1,000, respectively. The PSA also gave estimates for the relative decrease in new HCV infections over 10 years (30%, 95%CrI 18-44%) and 50 years (11%, 95%CrI 4-22%), and the relative decrease in HCV prevalence (21%, 95%CrI 13-30%) after 10 years, all compared to the counterfactual scenario, as shown in Table 5.

## Discussion

### Main findings

Replacing traditional HDSS with detachable LDSS through NSPs is likely to be a cost-saving strategy for reducing the transmission of HCV. These results were robust to all sensitivity analyses. Threshold analyses suggested that detachable LDSS would only need to reduce the risk of HCV transmission by 0.26% compared to HDSS to be cost-saving, and 0.04% to be cost-effective at a willingness-to-pay threshold of £20,000 per QALY gained as recommended by NICE.

### Strengths and limitations

This is the first analysis to evaluate the cost-effectiveness of using any type of detachable LDSS compared with HDSS. The key limitation of the analysis is the lack of direct evidence for the efficacy of detachable LDSS in reducing HCV transmission risk among PWID compared to HDSS. Better data is needed on this to determine the impact that using LDSS could have on reducing ongoing HCV and HIV epidemics. However, this uncertainty should not stop the expansion of using these syringes because our threshold analyses demonstrated that detachable LDSS would only have to result in a very small reduction in HCV transmission risk (compared to HDSS) of less than 1% for their use to be cost-saving.

The analysis solely focussed on Bristol. Although this may suggest the results are not generalisable, the incorporation of resource use and cost inputs from an ongoing intervention (by Bristol Drugs Project) means it is based on real data, whilst the robustness of the findings to extensive sensitivity analyses suggest its relevance to other settings. The evaluation of the targeted intervention in terms of prevention of HCV outcomes makes our analyses conservative, given that detachable LDSS may also

reduce the transmission of HIV and other blood borne viruses. The estimated reduction in healthcare costs and increase in QALYs could therefore be higher.

Several simplifying assumptions were made in relation to the transmission dynamics of HCV among PWID. Importantly, we did not incorporate heterogeneities in risk behaviour among PWID or restrictions in who they mix with. This is consistent with other economic evaluations of HCV treatment(21,23,38,39). It is known, however, that many PWID share injecting equipment with a restricted group of injection partners(40), and so HCV may spread rapidly within such groups without necessarily passing from one group to another. Although further analyses should consider how these complexities may affect the cost-effectiveness of detachable LDSS, the robustness of our findings suggest they are unlikely to change the conclusion that detachable LDSS are a highly cost-saving strategy for reducing the transmission of HCV.

Another uncertainty is in our understanding of how the cost-effectiveness of detachable LDSS may change with ongoing increases in HCV treatment uptake or reductions in treatment cost, which are occurring in many countries as they attempt to reach the WHO target of eliminating HCV as a public health threat by 2030(41). Our analyses suggest the use of detachable LDSS should remain highly cost-saving despite any changes in the costs and uptake of treatment, again emphasising the robustness of our results in the face of considerable unknowns.

## Implications and Conclusions

Despite uncertainty in the effectiveness of detachable LDSS, the results of our analysis suggest that the introduction of detachable LDSS through NSPs in Bristol is likely to be a cost-saving intervention that results in improved health outcomes. Because of the robustness of our findings, our results are likely to be generalisable to other regions of the UK and elsewhere. In many UK regions, detachable LDSS are not currently available, although in Scotland there has been a complete, unphased replacement of HDSS in response to an ongoing HIV epidemic(42). Wales has also rolled out detachable LDSS. In all settings, it is advised that to enhance the acceptability of detachable LDSS to service users, NSPs should transition gradually from distributing traditional HDSS to distributing detachable LDSS, while strongly encouraging and promoting their use to service users that currently use HDSS without alienating them. This should involve informing PWID of the reasons for their introduction(20). Unfortunately, uncertainty in the effectiveness of LDSS still hinders our understanding of the impact that this strategy could have if scaled up, and so the importance of detachable LDSS for controlling overall levels of HCV is unknown. Although well-designed studies are needed to obtain direct evidence of their effectiveness, these data are unlikely to change the conclusions of our analysis and so should not restrict the expansion of detachable LDSS in NSPs.

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## Tables

**Table 1:** Distribution of syringe types given out prior to and following the intervention

| Type of syringe used | Proportion used prior to targeted intervention (before 2016) | Proportion used following targeted intervention | | |
|---|---|---|---|---|
| | | 2016 | 2017 | 2018 onwards |
| Fixed LDSS | 62% | 62% | 62% | 62% |
| Detachable LDSS | 0% | 3% | 22% | 36% |
| HDSS (detachable) | 38% | 35% | 16% | 2% |
| % of detachable syringes that are LDSS* | 0% | 8% | 58% | 95% |

Abbreviations: HDSS, high dead space syringe; LDSS, low dead space syringe.

**Table 2:** Model parameters with their ranges for different sensitivity analyses

| Parameter | Point estimate | Range for sensitivity analysis | Rationale for range | Distribution for PSA† | Reference |
|---|---|---|---|---|---|
| ***Disease progression parameters*** | | | | | |
| Spontaneous clearance of HCV | 26% | 20% - 33% | +/-25% | Beta | (43) |
| Excess mortality in PWID vs. ex-PWID per year | 0.8% | 0.6% - 1.1% | +/-25% | Gamma | (22) |
| Treatment rate multiplier for PWID vs. ex-PWID | 0.54 | 0.41 – 0.68 | +/-25% | Normal | (36) |
| ***Annual transition probabilities‡*** | | | | | |
| Mild to moderate HCV | 2.5% | 1.8% - 3.3% | 95% CI | Beta | (21) |
| Moderate HCV to cirrhosis | 3.7% | 2.5% - 5.2% | 95% CI | Beta | (21) |
| Cirrhosis to decompensated cirrhosis | 3.9% | 3.0% - 8.3% | 95% CI | Beta | (21) |
| Cirrhosis to HCC | 1.4% | 0.2% - 3.9% | 95% CI | Beta | (21) |
| Decompensated cirrhosis to HCC | 1.4% | 0.2% - 3.9% | 95% CI | Beta | (21) |
| Decompensated cirrhosis to transplant | 3% | 1.2% - 5.6% | 95% CI | Beta | (21) |
| Decompensated cirrhosis to death | 13% | 11.1% - 15.0% | 95% CI | Beta | (21) |
| HCC to transplant | 3% | 1.2% - 5.6% | 95% CI | Beta | (21) |
| HCC to death | 43% | 37.2% - 48.9% | 95% CI | Beta | (21) |
| Transplant to death | 21% | 12.7% - 30.7% | 95% CI | Beta | (21) |
| Post-transplant to death | 5.7% | 3.7% - 8.2% | 95% CI | Beta | (21) |
| Mild HCV, moderate HCV or cirrhosis to SVR in ex-PWID* | 2.9% | 2.1% - 3.6% | +/-25% | Beta | (44) |
| SVR (cirrhosis) to decompensated cirrhosis (77% reduction compared to chronic infection transition probability) | 0.3% | 0.1% - 0.8% | 95% CI | Beta | (29) |
| SVR (cirrhosis) to HCC (78% reduction compared to chronic infection transition probability) | 0.3% | 0.2% - 0.5% | 95% CI | Beta | (28) |
| ***Syringe costs and distribution*** | | | | | |
| Fixed LDSS | £0.050 | £0.04 - £0.06 | +/-25% | Gamma | BDP |
| Detachable LDSS | £0.033 | £0.02 - £0.04 | +/-25% | Gamma | BDP |
| HDSS | £0.025 | £0.02 - £0.03 | +/-25% | Gamma | BDP |
| Annual number of syringes issued per PWID | 303 | 227.25 - 378.75 | +/-25% | Gamma | BDP |
| ***Annual cost of implementing targeted intervention*** | | | | | |
| Staff time | £536 | £402 -£670 | +/-25% | Gamma | BDP |
| ***Antiviral treatment costs*** | | | | | |
| 12-week course of sofosbuvir + ledipasvir | £15,000 | £11,250 - £18,750 | +/-25% | Gamma | Assumed cheaper than list price of £38,979.99 (45) |
| ***Annual cost of medical resource use*** | | | | | |
| Mild HCV | £87 | £63 - £105 | +/-25% | Gamma | (46) |
| Moderate HCV | £458 | £333 - £555 | +/-25% | Gamma | (46) |
| Cirrhosis | £714 | £519 - £865 | +/-25% | Gamma | (46) |
| Decompensated cirrhosis (infected or SVR) | £11,446 | £8,323 - £13,872 | +/-25% | Gamma | (46) |
| HCC (infected or SVR) | £10,198 | £7,416 - £12,360 | +/-25% | Gamma | (46) |
| Liver transplant (infected or SVR) | £46,164 | £33,570 - £55,949 | +/-25% | Gamma | (46) |
| Post-transplant | £2,131 | £1,548 - £2,580 | +/-25% | Gamma | (21) |

| | | | | | |
|---|---|---|---|---|---|
| Uninfected with SVR (mild HCV) | £313 | £228 - £380 | +/-25% | Gamma | (23) |
| Uninfected with SVR (moderate HCV) | £916 | £666 - £1,110 | +/-25% | Gamma | (46) |
| Uninfected with SVR (cirrhosis) | £1,428 | £1,038 - £1,731 | +/-25% | Gamma | (46) |
| ***Health state utility values*** | | | | | |
| Uninfected (PWID) | 0.85 | 0.80 - 0.90 | As in (21) | Beta | (21) |
| Uninfected (ex-PWID) | 0.90 | 0.85 - 0.95 | As in (21) | Beta | (47) |
| Mild HCV | 0.77 | 0.74 - 0.80 | 95% CI | Beta | (46) |
| Moderate HCV | 0.66 | 0.60 - 0.72 | 95% CI | Beta | (46) |
| Cirrhosis | 0.55 | 0.44 - 0.65 | 95% CI | Beta | (46) |
| Decompensated cirrhosis (infected or SVR) | 0.45 | 0.39 - 0.51 | 95% CI | Beta | (46) |
| HCC (infected or SVR) | 0.45 | 0.39 - 0.51 | 95% CI | Beta | (46) |
| Liver transplant (infected or SVR) | 0.45 | 0.39 - 0.51 | 95% CI | Beta | (46) |
| Post-transplant (infected or SVR) | 0.67 | 0.53 - 0.79 | 95% CI | Beta | (46) |
| Uninfected with SVR (mild HCV) | 0.82 | 0.62 - 1.03 | +/-25% | Beta | (48) |
| Uninfected with SVR (moderate HCV) | 0.72 | 0.54 - 0.90 | +/-25% | Beta | (48) |
| Uninfected with SVR (cirrhosis) | 0.60 | 0.45 - 0.75 | +/-25% | Beta | (48) |
| ***Utility decrements*** | | | | | |
| Antiviral treatment | 0.06 | 0.05 - 0.08 | +/-25% | Beta | (49) |

† All distribution parameters are estimated assuming that the 'range for sensitivity analysis' represents the 95% confidence interval.

‡ All transition probabilities converted to instantaneous rates for use in the model.

* Calculated as the treatment rate (3%) multiplied by the sustained viral response rate (95%).

**Abbreviations**: BDP, Bristol Drugs Project; CI, confidence interval; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HDSS, high dead space syringe; LDSS, low dead space syringe; PWID, people who inject drugs; SVR, sustained viral response.

**Table 3**: Relative infectiousness of different syringe types following contamination with HCV virus; including data from Binka et al. Plos one 2015 (8) and estimates derived from that study.

| **Type of syringe** | **Percentage with detectable virus** | **Residual infectivity*** | **Infectivity measure**** |
|---|---|---|---|
| Fixed LDSS (27G½" gauge) | 47% (42/90) | 4978 ± 3570 | 2323.1 |
| Detachable HDSS (23G1¼" gauge) | 95% (57/60) | 9861 ± 7026 | 9368.0 |
| Detachable HDSS (25G" gauge) | 88% (53/60) | 9339 ± 6841 | 8249.5 |
| Detachable LDSS (23G1¼" gauge) | 65% (39/60) | 7127 ± 5406 | 4632.6 |
| Detachable LDSS (25G" gauge) | 80% (48/60) | 5724 ± 4014 | 4579.2 |

*The residual infectivity or quantity of detectable virus was estimated using luminescence measurements in relative luciferase units (RLUs), as given out by the virus – see Binka et al. (8) for more details. The range is the standard deviation around the mean measure as given in Binka et al;
**Infectivity measure is the product of the percentage of syringes that are detectable and the average quantity of detectable virus in these syringes.

**Table 4:** Difference in costs (total and disaggregated) and QALYs for the intervention (detachable LDSS were distributed) and counterfactual scenario (detachable LDSS were not distributed) over 50 years

| | **Counterfactual scenario** | **Intervention scenario** | **Incremental difference in costs and QALYs** |
|---|---|---|---|
| Syringe costs | £840,104 | £857,136 | £17,032 |
| Implementation costs | £0 | £4,685 | £4,685 |
| HCV treatment costs | £17,189,423 | £15,362,552 | -£1,826,871 |
| HCV-related care costs | £26,567,508 | £24,256,260 | -£2,311,248 |
| **Total costs** | **£44,597,035** | **£40,480,634** | **-£4,116,401** |
| **Total QALYs** | **136,397** | **137,398** | **+1,000** |

**Abbreviations**: HCV, hepatitis C virus; QALY, quality-adjusted life-year.

**Table 5:** Results of probabilistic sensitivity analysis for the costs and impact of the intervention. Range in brackets is the 95% credibility interval, defined as the 2.5 to 97.5 percentile range, and M denotes million.

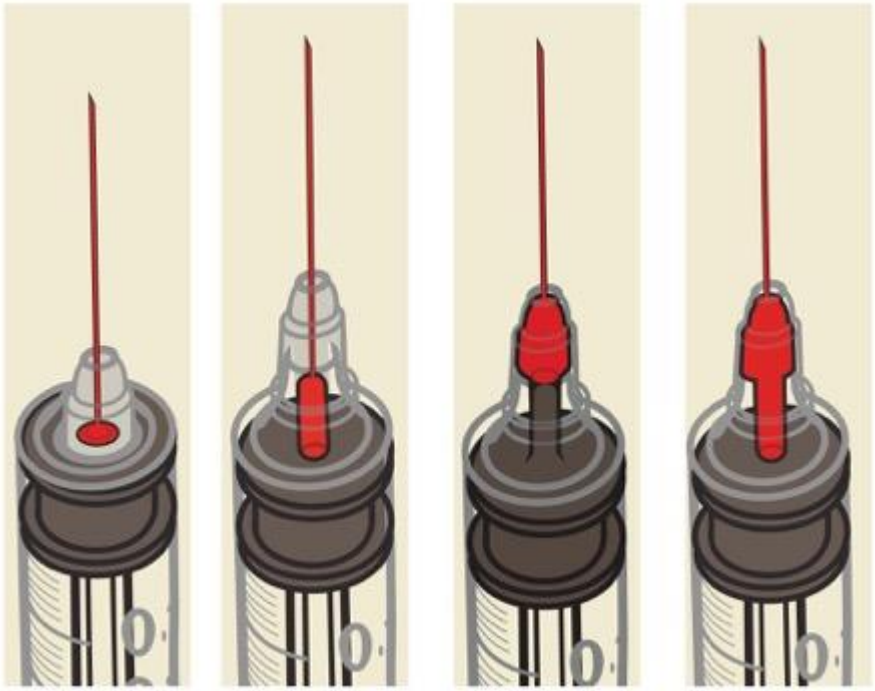
| **Outcome** | **Counterfactual scenario** | **Intervention scenario** | **Incremental difference** | **% decrease*** |
|---|---|---|---|---|
| Total costs | £44,125,862 (£31.2 to 61.8M) | £40,229,109 (£28.4 to £57.1M) | -£3,896,754 (-£6.3 to -£2.1M) | |
| Total QALYs | 136,613 (114,523 to 161,803) | 137,563 (115,336 to 162,749) | 951 (455 to 1,635) | |
| Number of new infections over 10 years | 1,092 (637 to 1718) | 772 (400 to 1306) | -320 (-523 to -175) | 30% (18% to 44%) |
| Number of new infections over 50 years | 5,149 (2,066 to 9,127) | 4,661 (1,678 to 8,628) | -488 (-790 to -265) | 11% (4% to 22%) |
| Prevalence of infection after 10 years | 38% (26% to 52%) | 30% (21% to 43%) | -8% (-12% to -4%) | 21% (13% to 30%) |

* % decrease in the outcome for the intervention scenario compared to the counterfactual scenario

**Figures**

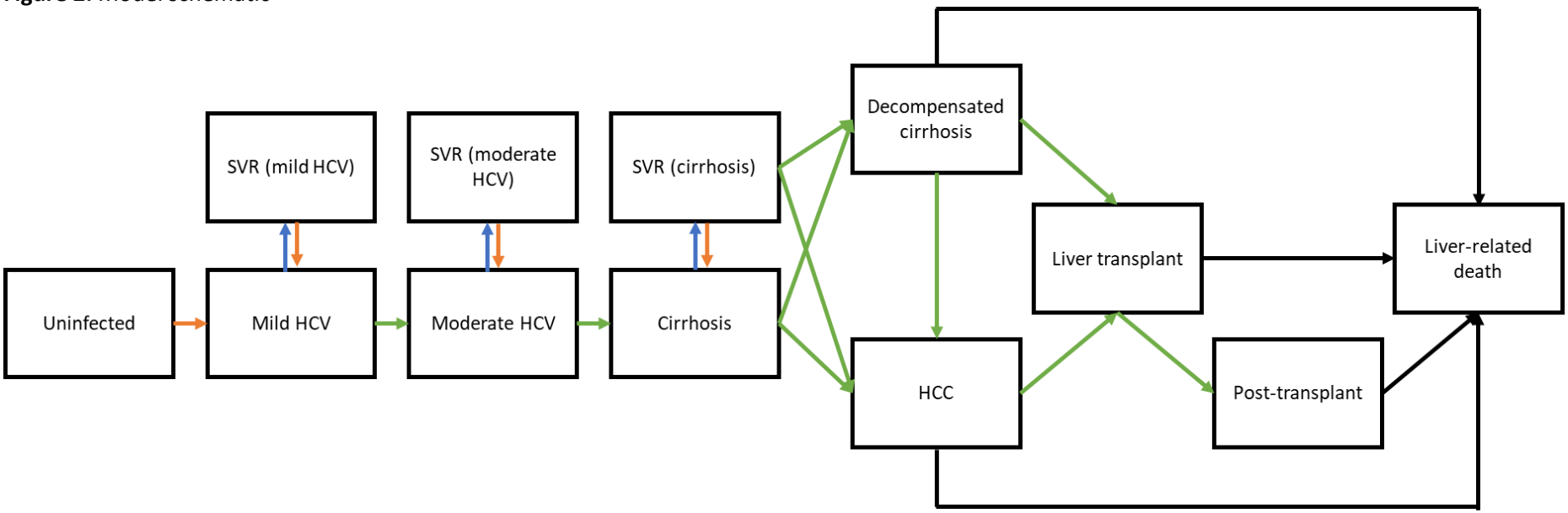
**Figure 1.** Illustration of the dead space in different needle and syringe combinations.

Produced by NIHR CLAHRC West, NIHR HPRU in Evaluation of Interventions at University of Bristol, Bristol Drugs Project, Linnell Communications, Exchange Supplies and Public Health England. This work was supported by the Economic and Social Research Council – Grant ES/M500410/I



| Low dead space fixed needle and syringe | Low dead space detachable needle | Reduced dead space modified syringe with detachable needle | Traditional high dead space detachable needle and syringe |
|---|---|---|---|

**Figure 2:** Model schematic†



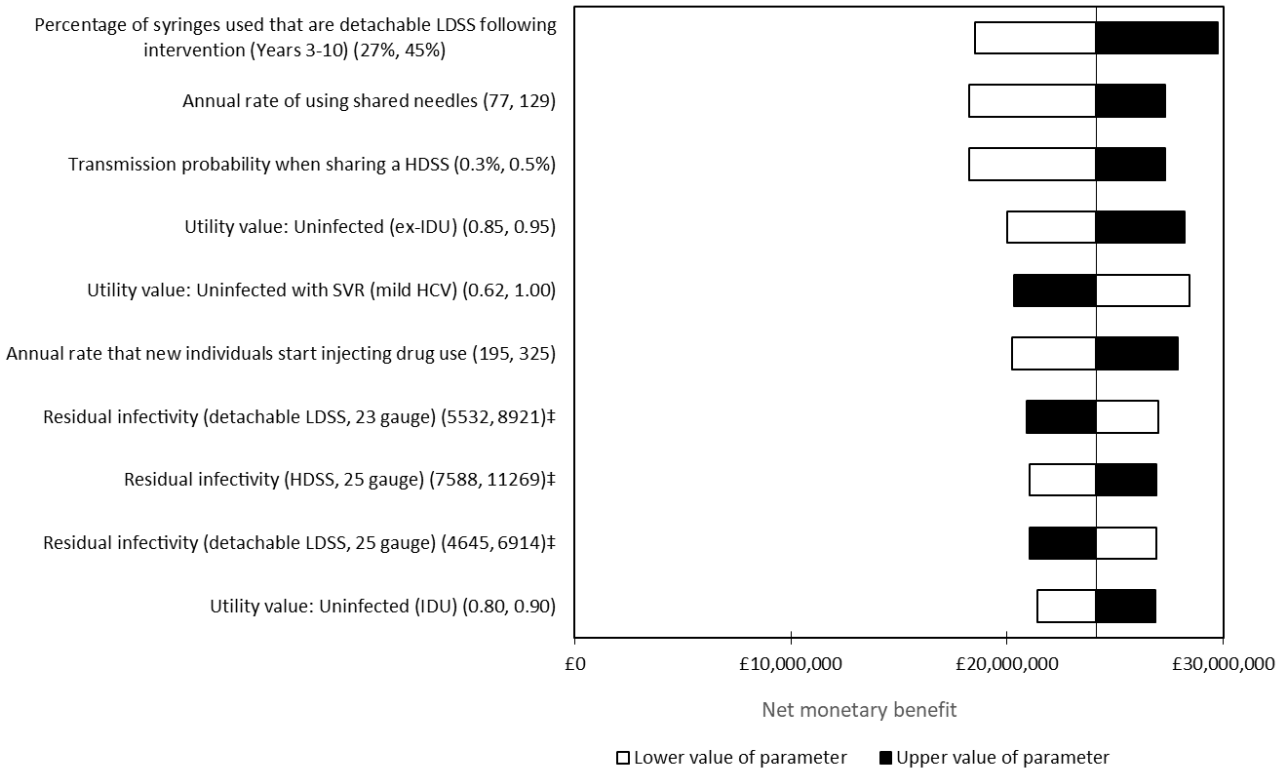

† Non-liver-related death may occur from all model health states.

**Key to arrows: Orange = Infection; Blue = Successful treatment; Green = Progression; Black = Death.**

**Note**: progressions states beyond cirrhosis are duplicated for those that are infected and those that have achieved SVR and are uninfected.

**Abbreviations**: HCC, hepatocellular carcinoma; HCV, hepatitis C virus; SVR, sustained viral response.

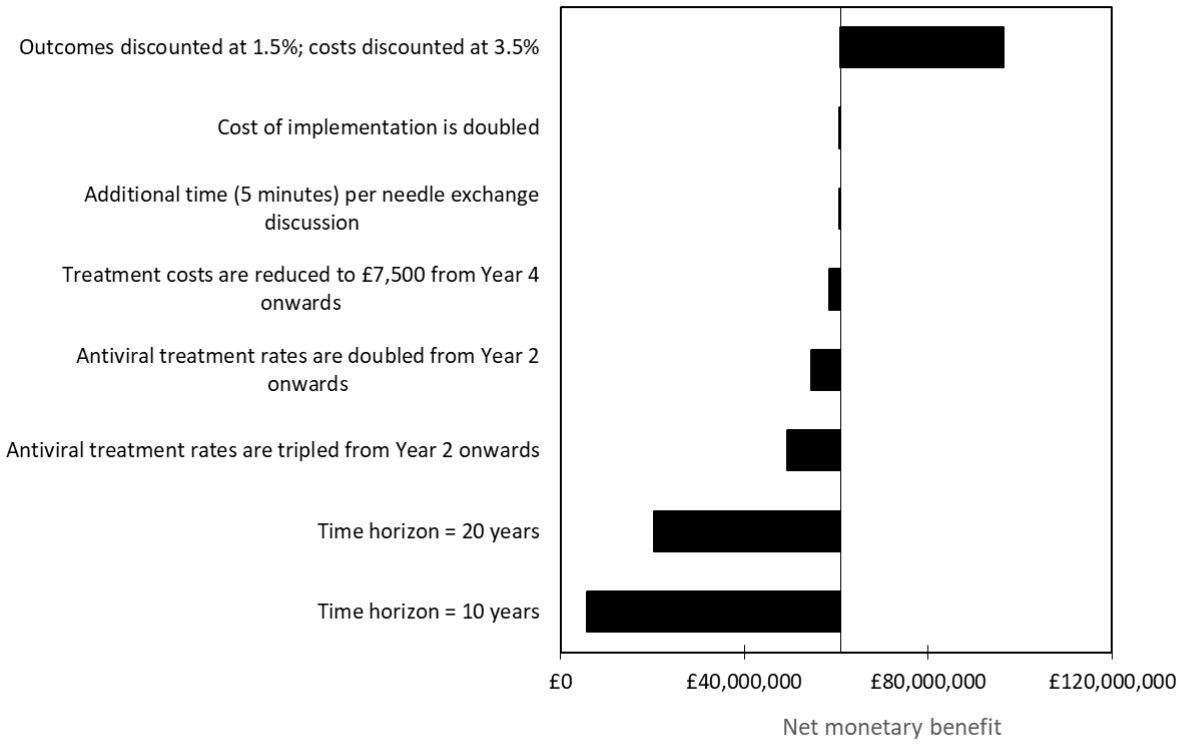
**Figure 3:** Tornado diagram† for univariate sensitivity analysis where each parameter is varied +/-25% or across their 95% confidence intervals where available‡




† The vertical axis is centred on the base-case net monetary benefit; ‡ Estimates of the 95% confidence interval were used.

**Abbreviations**: HCV, hepatitis C virus; IDU, injecting drug user; HDSS, high dead space syringe; LDSS, low dead space syringe; SVR, sustained viral response.

**Figure 4: Tornado diagram for scenario analysis**




**Abbreviations**: LDSS, low dead space syringe.